"ECHOCARDIOGRAPHIC EVALUATION OF PAPILLARY MUSCLE FUNCTION IN ISCHEMIC MITRAL REGURGITATION"

Dissertation submitted for

D.M. DEGREE EXAMINATION

BRANCH II – CARDIOLOGY

MADRAS MEDICAL COLLEGE

AND

GOVERNMENT GENERAL HOSPITAL

CHENNAI – 600 003

THE TAMIL NADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI – 600 032

AUGUST 2007

CERTIFICATE

This is to certify that the dissertation entitled **"ECHOCARDIOGRAPHIC EVALUATION OF PAPILLARY MUSCLE FUNCTION IN ISCHEMIC MITRAL REGURGITATION"** is the bonafide original work of **Dr.P.JAISANKAR**, in partial fulfillment of the requirements for D.M. Branch-II (CARDIOLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2007.The period of post-graduate study and training was from August 2004 to July 2007.

THE DEAN

MADRAS MEDICAL COLLEGE

AND

GOVERNMENT GENERAL HOSPITAL

CHENNAI - 600 003.

PROFESSOR V.JAGANATHAN M.D., D.M.

PROFESSOR AND HEAD OF THE DEPARTMENT OF CARDIOLOGY

MADRAS MEDICAL COLLEGE

AND

GOVERNMENT GENERAL HOSPITAL

CHENNAI - 600 003.

DECLARATION

I **Dr.P.JAISANKAR,** solemnly declare that this dissertation entitled, **"ECHOCARDIOGRAPHIC EVALUATION OF PAPILLARY MUSCLE FUNCTION IN ISCHEMIC MITRAL REGURGITATION"** is a bonafide work done by me at the department of Cardiology, Madras Medical College and Government General Hospital during the period 2004 – 2007 under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital, Professor V.Jaganathan M.D.D.M. This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards partial fulfillment of requirement for the award of **D.M. Degree (Branch-II) in Cardiology.**

Place : Chennai

Date:

Dr.P.JAISANKAR

ACKNOWLEDGEMENTS

A great many people made this work possible. I thank my Dean

for allowing me to conduct this study.

My warmest respects and sincere gratitude to our beloved ***Prof V.Jaganathan*** *Professor and Head of the Department of Cardiology, Government General Hospital, Chennai who was the driving force behind this study. But for his constant guidance this study would not have been possible.*

My respectful thanks to ***Prof R.Alagesan*** *for his constructive ideas, personal guidance and involvement in this study.*

I am indebted to ***Prof. Geetha Subramanian, Prof A.Balaguru, Prof. B.Ramamurthy and Prof. P.Arunachalam*** *without whom, much of this work would not have been possible.*

I acknowledge ***Dr M.A.Rajasekar*** *for the many useful comments he made during this project.*

*In addition, I am grateful to****, Dr. G.Gnanavelu, Dr.D.Muthukumar, Dr.G.Karthikeyan, Dr.G.Palanisamy, Dr.P.S.Mohanamurugan Dr S.Venkatesan Dr.K.Meenakshi, Dr.G.Ravishankar, , Dr.Murthy, Dr.P.Justin Paul*** *for tracing all those waveforms and guidance.*

I am thankful to my wife ***DR.J.PRIYA*** *for her support, understanding and for the help concerning the computer network.*

Last but not the least I thank all my patients for their kind cooperation.

CONTENTS

"learn to heal"

INTRODUCTION

Ischemic mitral regurgitation is defined as mitral regurgitation due to coronary artery disease with structurally normal mitral valve leaflet and chordae. Some authors prefer to use the term as functional mirtal regurgitation [1]. But functional mitral regurgitation can occur in idiopathic dilated cardiomyopathy without coronary artery disease. So Ischemic mitral regurgitation and functional mitral regurgitation are not synonymous.

The incidence of coronary artery diseases in rural and urban population in India is reported to be between 14.8 per thousand to 65.4 per thousand[2]. Patients with coronary artery diseases during their course may develop complications such as arrhythmias, mechanical complications (ventricular septal rupture, Ischemic mitral regurgitation) and pump failure.

Ischemic mitral regurgitation occurs in approximately 20% of patients after myocardial infarction and 56% of patients with heart failure due to ischemic or non ischemic cardiomyopathy. [3, 4] Ischemic mitral regurgitation can occur in coronary artery disease both during acute phase and chronic phase. Ischemic mitral regurgitation is more common in inferior wall myocardial infarction than anterior wall myocardial infarction.[5] There is a graded independent association between the severity of ischemic MR and the development of Heart failure after myocardial infarction. Even mild ischemic MR is associated with an increase in the risk of heart failure. Ischemic mitral regurgitation is an independent prognostic factor in patients with chest pain even without myocardial infarction. [6] Advancing age, female gender, multiple vessel coronary artery disease, congestive heart failure, recurrent ischemia, large infarct size, and prior acute myocardial infarction are all risk factors for developing IMR.

MITRAL REGURGITATION (MR)

Is the regurgitation of blood from left ventricle to left atrium during systole due to inadequate cooptation of mitral leaflet. Mitral regurgitation is caused by several diseases. In India Rheumatic fever is the leading cause of Mitral Regurgitation. As the incidence of RF is declining recently, Mitral Regurgitation due to other causes also contributes considerably.

Causes of Chronic Mitral Regurgitation; [7]

INFLAMMATORY

Rheumatic heart disease

Systemic lupus erythematosus

Scleroderma

Degenerative

Myxomatous degeneration of mitral valve leaflets (Barlow click murmur syndrome, prolapsing leaflet, mitral valve prolapse)

Marfan syndrome

Ehlers-Danlos syndrome

Pseudoxanthoma elasticum

Calcification of mitral valve annulus

INFECTIVE

Infective endocarditis

STRUCTURAL

Ruptured chordae tendineae

Rupture or dysfunction of papillary muscle

Dilation of mitral valve annulus and left ventricular cavity.

HOCM (Hypertrophy obstructive cardiomyopathy)

Prosthetic Paravalvular leak.

CONGENITAL

Mitral valve clefts or fenestrations

Parachute mitral valve abnormality in association with

1. Endocardial cushion defects
2. Endocardial fibroelastosis
3. TGA (D Transposition of great artery)
4. ALCOPA (Anomalous origin of left coronary from pulmonary artery)

ISCHEMIC MITRAL REGURGITATION (IMR)

Ischemic MR is a common complication of ischemic heart disease as mentioned above and it adversely affects the prognosis. [8, 9]

Mechanism of IMR

While acute MR secondary to rupture of the PM is well understood, the understanding of the development of IMR in ventricular dysfunction is not totally clear [1]. **Mitral annular dilatation** may play an important role in IMR. During systole the mitral valve annulus is usually smaller than in diastole. Mitral annulus size is reduced by 20 – 30% during systole. Combined with the redundant mitral valve leaflet overlap, this prevents regurgitation. Mitral annular dilatation is usually the result of ventricular enlargement. When the dilatation is large enough to overcome the normal area of redundant

leaflet overlap MR will develop. This mechanism is similar in patients with non ischemic cardiomyopathy who develop MR.[10] The concept that MITRAL ANNULAR DILATATION causes functional mitral regurgitation was created **i**n 1956 by *DR. Friedberg***.**[11] But the first clinical study to assess the mitral annular dilatation as the cause of IMR came from *DR.BOLTWOOD et al* in1983.[12] When they sought to elucidate the mechanism of mitral regurgitation (MR) in dilated cardiomyopathy(DCM). One decade later *BOLTWOOD* was supported by *DR SHENGQIN HE et al* in 1997 and he concluded that annular dilatation increases regurgitation for any position of PM and creating clinically significant MR[13]

In contrary to above studies *DR.YATAKA OTSUJI et al* in 2002 said that Isolated Annular Dilation Does Not Usually Cause Important Functional Mitral Regurgitation. and he proved that in human studies.[14].

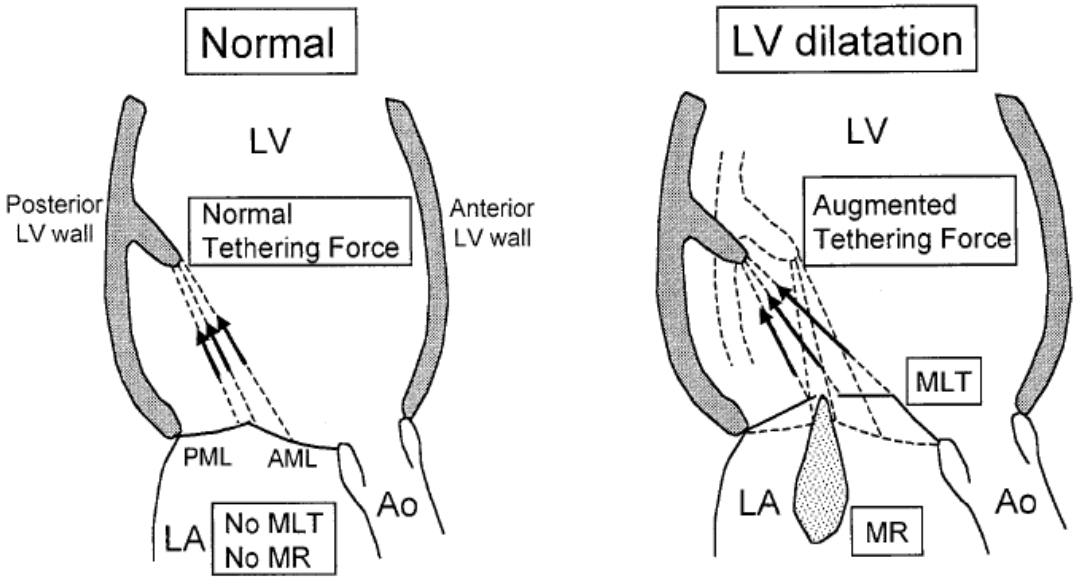
Papillary Muscle Displacement and LV Geometry

Recent work in both animal and human studies has examined the role of global and regional ventricular dysfunction in PM displacement. When the Papillary muscles are displaced towards the LV apex, it causes tenting of the leaflet. Leaflet tenting pulls the tips of the mitral leaflets away from each other; resulting in less leaflet overlap and development of MR. This leaflet tethering is measured as leaflet tethering distance. All the studies in the past demonstrated consistent correlation of increased leaflet tethering distance with ischemic mitral regurgitation.

Several studies suggest that global change in the geometry of the left ventricle results in IMR. LV remodeling causes sphericalization of the left ventricle leading to apical displacement of both papillary muscles. This results in chordal tethering leading to the failure coaptation of the mitral valve leaflets. In addition, global LV dilatation also leads to annular dilatation which exacerbates the degree of MR. Several authors have also suggested that impairment of LV systolic function results in a decrease in the generation of force needed to close the mitral leaflets, thereby compounding the issue [15,

[16]. The impact of global dilatation was illustrated in a canine model of infarction where the pericardial space was reduced by folding the pericardium over itself parallels to the long axis and suturing it to limit LV dilatation[17]. Then the left circumflex artery was ligated, producing ischemia of the infero-posterior wall and medial PM. With restriction of LV dilatation, there was no MR. However when the LV was allowed to dilate, MR developed. Three-dimensional echocardiography demonstrated an increased tethering distance from the PM to the anterior annular ring. The tethering length correlated with LV sphericity.[18]

However, not all patients with global LV dilatation develop MR [19]. In addition the same amount of LV dysfunction is associated with varying degrees of MR.[20] *Kono et al* demonstrated that changes of LV geometry due to the regional hyperkinesias of the LV segment overlying the PM may play an important role in the development of IMR[1]. In a canine model of acute MI, they demonstrated that changes in the configuration of the left ventricle can affect the position of one or both papillary muscle groups. Remodeling of the inferior basal wall caused apical displacement of the papillary muscles. This resulted in significant increase in the distance between the coaptation point of the mitral valve leaflets and the plane of the mitral valve resulting in IMR [1]. In contrast, global models of IMR showed no correlation between an increase in LV volumes and degree of MR . Thus apical displacement of the PM as a result of changes in the regional LV dysfunction is sufficient to cause IMR.



In patients with LV dysfunction, *Yia* used quantitative echocardiography to determine the relationship between the degree of functional mitral deformation and local ventricular remodeling.[20] they found that the major determinant of effective regurgitant orifice (ERO) of IMR was the degree of systolic mitral tenting, and to a lesser extent, systolic mitral tenting was directly related to local remodeling that caused apical and posterior displacement of both PM. Lateral displacement of the PM was only weakly associated with the degree of IMR. The displacement of the PM was independent of LV global remodeling, Ejection Fraction, LV volume and sphericity.

The observation that ischemia worsened MR led to the term PM dysfunction".[21] However, an alternative hypothesis suggests that PM ischemia may in fact result in a decrease in MR by displacing the leaflets towards the annulus due to elongation of the ischemic PM.[22, 23] This was demonstrated by Messas et al in a sheep model of acute MI with and without PM ischemia. Inducing ischemia of the inferior basal wall with preserved perfusion of the PM resulting in the development of IMR. As the chordal tethering length increased, the degree of IMR increased suggesting that the protective role of overlap of redundant leaflet tissue was no longer available;. When papillary muscle ischemia was added, the degree of IMR and ERO decreased despite a further decrease in systolic

function and increased annular dilatation. The papillary muscle was shown to elongate and the PM tip moved closer towards the annulus. This decreased chordal tethering length resulting in a more effective leaflet coaptation and a reduction in IMR. The experimental and clinical data emphasize the importance changes in the geometry of the LV that result in IMR. Mitral annular dilatation and the apical displacement of the normally functioning PM may play a separate or additive role in the pathogenesis of IMR.

REVIEW OF LITERATURE

First, we will briefly review about the functional anatomy of mitral valve apparatus.

FUNCTIONAL ANATOMY OF MITRAL VALVE; [24, 25]

THE MITRAL APPARATUS is a complex - finely coordinated mechanism that can be deranged by a multiplicity of acquired and congenital disorders and requires competence for its functional integrity of six elements working in delicate concert.[26] These anatomic elements are: (1) left atrial wall, (2) annulus, (3) leaflets, (4) chordae tendineae, (5) papillary muscles, and (6) left ventricular wall.

The exact mode of closure of the normal mitral valve is still uncertain.[27, 28] Left ventricular systole begins with contraction of the papillary muscles. The vertical forces exerted by the contracting papillary muscles move the leaflets into apposition. As the intraventricular pressure rises, the free edges of the cusps firmly coapt, mutually supporting each other along a comfortable margin of their atrial surfaces, and firmly sealing the orifice. The remainder of each leaflet bulges like a parachute toward the left atrium.[29] The annulus not only serves as a fulcrum for the leaflets, but during ventricular systole decreases its circumferential size, thus reducing the area that the leaflets are required to bridge.[30, 31] Even so, the surface area of the leaflets is about two and half times the area of the orifice, thus providing a comfortable reserve. As the left ventricle ejects, its apex and the mitral orifice approach each other. Shortening of the vertical axis of the left ventricle is accompanied by synergistic contraction of the papillary muscles and adjacent left ventricular wall so that an appropriate vertical anchoring force is applied to the chordae tendineae that prevents the eversion of leaflets. Let us now turn our attention to the six anatomic components of the mitral apparatus which when faulty can disturb

the harmony of the valvular mechanism and render it incompetent. Coordinated interaction among these elements-which are interdependent- usually means that more than one, or even several, are deranged at any one

LEFT ATRIUM

Two contributions of the left atrium have been related to competence of the mitral valve: (1) contraction and relaxation [32, 33] and (2) atrial dilatation. Although atrial contraction and relaxation seem to be capable of closing the mitral valve in man, the absence of such activity does not cause mitral regurgitation.[34] Competence of the mitral apparatus depends in part on a normal sequence of ventricular activation but not on a normal sequence of atrial and ventricular contraction. Loss of effective atrial contraction (atrial fibrillation, complete heart block, and others) does not necessarily result in regurgitation. [34] Left atrial enlargement itself can contribute to mitral regurgitation. Dilatation of the left atrium does not affect the anterior leaflet since that leaflet is anchored to the root of the aorta. The posterior leaflet, however, can be directly affected.[29] As the left atrium enlarges, its posterior wall is displaced posteriorly and downward. Because of the continuity of the atrial endocardium and posterior mitral leaflet, this displacement exerts tension on the posterior leaflet.[29] The displacement may prevent that cusp from contacting its mate or may aggravate preexisting leaflet malapposition. Thus, as mitral regurgitation provokes left atrial enlargement, as Edwards and Burchell[35] aptly put it, "mitral insufficiency begets mitral insufficiency" irrespective of the initiating causes.

MITRAL ANNULUS

The annulus forms an important part of the basal attachment or fulcrum of the mitral leaflets.[29,35] A traditional point of view states that if the atrioventricular ring dilates sufficiently, the cusps are unable to meet and mitral regurgitation results." This explanation is an oversimplification. Left ventricular dilatation - an undoubted cause of mitral incompetence-may exert its effects independently

of dilatation of the mitral ring. Nevertheless, the size of the ring does play a role in preserving competence of the mitral valve, albeit a role that relates less to dilatation than to failure to decrease its circumference during systole. The tissue at the basal attachments of the mitral leaflets is tough but pliable. Toughness opposes dilatation; pliability permits sphincter-like contraction of the annulus during systole, which reduces the area that the apposing leaflets must bridge by an estimated 20 to 50%.[27,31] Left ventricular dilatation may exert an unfavorable effect on the annulus chiefly by applying a distending pressure that opposes systolic annular contraction.

MITRAL LEAFLET

Proper closure of the leaflets represents an ultimate goal of the entire mitral mechanism. The areas of the two leaflets are nearly identical, but the basal to free edge length of the anterior leaflet is two or more times that of the posterior leaflet. Consequently, the anterior leaflet is more mobile, while the posterior leaflet fulfills a secondary or supporting role."[36] Although the mitral leaflets, like other cardiac valves, have been looked upon as passive connective tissue structures, recent investigations have found within their substance striated muscle bundles to which an active function has been assigned.[37]. It is uncertain whether such muscle fibers have physiologic significance in promoting closure of the valve.

PAPILLARY MUSCLE AND CHORDE TENDINAE

Functional anatomy of the normal papillary muscle: [24]

There are two groups of papillary muscles in the left ventricle, the anterolateral group and the posteromedial group. The anterolateral papillary muscle arises from the anterolateral wall of the left ventricle and receives its blood supply primarily from marginal tributaries of the circumflex branch of the left coronary artery.[24] In some hearts, the anterolateral papillary muscle receives a secondary blood

supply from the anterior descending branch of the left coronary artery. The posteromedial papillary muscle arises near the junction of the posterior wall of the left ventricle and the Interventricular septum and is supplied with blood either by tributaries from the circumflex artery or by posterior descending branches from the right coronary artery These small papillary arteries course longitudinally to the apex of the papillary muscle where they terminate in the arterioles, capillaries, venules, and small veins. At times these papillary arteries form arcuate anastomoses near the distal ends of the muscle. In the normal-sized heart, the long axis of the papillary muscle is oriented almost perpendicular to the atrioventricular ring. This orientation of the papillary muscles provides a mechanical advantage in that tension developed by the papillary muscles is applied almost perpendicular to the mitral valve leaflets. On the other hand, with ventricular dilatation the papillary muscles migrate laterally, so that tension developed by the papillary muscles is applied tangentially to the mitral leaflets. The greater the lateral displacement of the papillary muscles the greater the mechanical disadvantage. The function of the papillary muscles and chordae tendineae to restrain the movements of the mitral valve leaflets during ventricular systole is obvious. However, the dynamic nature of this function is not always appreciated. Normal mitral valve function depends upon the maintenance of the proper spatial relationships between the papillary muscles, the chordae tendineae, and the mitral valve leaflets throughout all phases of the cardiac cycle. During the isovolumetric phase of ventricular systole the rapid rise in intraventricular pressure causes the mitral valve leaflets to bulge towards the left atrium and to come into firm surface contact with each other, thus closing the atrioventricular orifice.[38-41] The movement of the mitral valve leaflets towards the atrium pulls the chordae tendineae taut. In the interest of completeness, it may be stated that there is evidence that the mitral valve leaflets come into apposition to close the atrioventricular orifice just before the onset of ventricular systole.[42] Nevertheless, firm apposition of the leaflets probably does not occur until the onset of isovolumetric contraction, at which time the two opposing forces of intraventricular pressure and papillary muscle tension assure that the portions of the mitral leaflets which are in apposition are tightly sealed. It should be understood that the chordae

tendineae from each papillary muscle attach to the corresponding halves of both leaflets of the mitral valve. The papillary muscles and chordae tendineae must support the force acting upon the mitral valve, which is equal to the intraventricular pressure times the cross-sectional area of the atrioventricular orifice. In a previous report from this laboratory,[43] we have estimated, on the basis of certain theoretic considerations, that each papillary muscle of the left ventricle supports a total peak load of 19 tons during a 24 hour period for a heart rate of 70 beats per minute and an arterial blood pressure of 120/80 mm. Hg.

During the ejection phase of ventricular systole, the apex of the left ventricle moves towards the atrioventricuIar orifice. Since the moment-to-moment length of the chordae tendineae is fixed, the papillary muscles must shorten during systole to maintain the proper distance between the base of the papillary muscles and the atrioventricular orifice in order to prevent eversion of a portion of the mitral leaflets into the left atrium. It is of interest that motion pictures of mitral valve movement in the intact dog have demonstrated that the mitral valve leaflets move downward into the ventricle during ventricular systole rather than upward toward the atrium.[44] Thus, contraction of the papillary muscles takes up the slack which would have been created in the chordae tendineae as a result of the shortening of the distance between the apex of the left ventricle and the atrioventricular orifice during the ejection phase of ventricular systole. Furthermore, the papillary muscles must develop sufficient tension to overcome intraventricular pressure. This latter point is important since the tension in the free wall of the left ventricle decreases or remains constant during the ejection phase of systole[45]. Therefore, while the muscle of the free wall of the left ventricle “loafs” during ventricular ejection, the papillary muscles must continue to develop more tension.

Since 1968, when *DR.G.E BURCH et al*[25] first described the ‘syndrome of papillary muscle dysfunction ‘ the contribution of papillary muscle dysfunction to the pathogenesis of ischemic mitral regurgitation is, up to date still controversial. In his essay, he elaborately discussed the

papillary muscle dysfunction and its manifestation. He enumerated the causes of PM dysfunction as follows;

Etiology of papillary muscle dysfunction [25]

1. Circulatory insufficiency (ischemia)

    Angina pectoris

    Infarction of papillary muscle

    Acute

    Chronic (fibrosis)

    Systemic circulatory disturbances (hypotension, erythrocytosis, anoxia, hematometakinesia, etc.)

2. Left ventricular dilatation

    Generalized

    Localized (aneurysm)

3. Non ischemic atrophy of papillary muscle

    Senile

    Associated with cachexia

4. Defective development of papillary muscle apparatus

    Congenitally long or short papillary muscle or

    chordae tendineae

    Ectopic origin of papillary muscle

    Ectopic insertion of chordae tendineae

5. Endocardial disease

    Endocarditis

Endocardial fibroelastosis

Endomyocardial fibrosis

6. Heart muscle disease

Inflammatory (myocarditis)

Degenerative cardiomyopathy

Infiltrative (metastatic carcinoma, amyloidosis)

7. Neoplastic (primary tumor of myocardium)

Disturbances in the time course of papillary muscle

activation and contraction

8. Rupture of papillary muscle or chordae tendinea

The most common causes of PM dysfunction is coronary insufficiency. Papillary muscle is vulnerable to ischemia because; [24,25]

Papillary muscle is subendocardial structures,

Papillary muscle are supplied by terminal branches of the coronary arteries,

Papillary muscle is the thickest portion of the endocardium.

Papillary muscle develop large amounts of tension during ventricular systole,

These factors combine to render the papillary muscles particularly vulnerable to ischemia. The papillary muscles may become ischemic not only as a result of narrowing of the coronary arteries but also as a result of disease states associated with diminished coronary artery perfusion. Because of the large amounts of tension which must be developed by the papillary muscles during ventricular systole, they are easily damaged by ischemia. Furthermore, in some hearts the major blood supply to both papillary muscles of the left ventricle is derived from the same artery (circumflex branch of left coronary artery), so that the risk of simultaneous ischemia of both papillary muscles is increased.

The great vulnerability of the papillary muscles to ischemic damage is emphasized by the fact that one or both papillary muscles showed evidence of recent or old infarction in 25 per cent of 422

consecutive hearts studied at necropsy[46]. During episodes of ischemia or following infarction of a papillary muscle, the muscle is rendered completely or partially incapable of contraction. Providing that the heart is not enlarged, the normal spatial relationships between the elements of the mitral valve apparatus are maintained during isovolumetric contraction and the valve is competent However, during ventricular ejection the slack created in the chordae tendineae by the apex-to-base movement of the left ventricle is not taken up because of the inability of the ischemic papillary muscle to shorten. Thus, a portion of each mitral valve leaflet everts into the left atrium and the valve becomes incompetent if the ischemia is only transitory, as during an episode of angina pectoris, clinical evidence of mitral valve incompetence rapidly subsides as the ischemic papillary muscle regains the ability to contract. On the other hand, following infarction of a papillary muscle, the clinical signs of mitral incompetence usually regress slowly as the papillary muscle gradually recovers. The changing characteristics of the murmur associated with papillary muscle dysfunction as a result of infarction of the muscle will be explained on this basis. It should be pointed out, however, that the sudden development of an apical systolic murmur after myocardial infarction is much more often due to papillary muscle dysfunction than to rupture of a papillary muscle or perforation of the interventricular septum. When ischemia and/or infarction results in diffuse scarring, degeneration, and atrophy of a papillary muscle, the retracted muscle pulls a portion of each mitral leaflet into the ventricle so that the valve is incompetent even during isovolumetric contraction. During the ejection phase of systole, the apex-to base movement of the left ventricle may permit better apposition of the mitral valve leaflets so that the degree of valve incompetence decreases.

In contrary to elaborate discussion of Papillary muscle dysfunction by previous author, in 1991 *DR.SANJIVE KAUL et al*,[47]did an experimental work with dogs and concluded that PMD and/or dysfunction of the immediately adjacent LV myocardium does not result in MR. MR occurs during ischemia only when global LV function is affected, even when thickening of the papillary muscles and the immediately adjacent LV remains intact. MR in this situation is related to Incomplete Mitral Leaflet

Coaptation {IMLC}; the greater the degree of IMLC, the greater the MR. These findings suggest that the mechanism of ischemic MR is not related to PMD. There may also be important therapeutic implications of these findings. In his study dogs were grouped as follows, group 1 dogs (n=8), varying degrees of regional and global LV dysfunction were produced. In group 2 dogs (n=7), the circulation to the papillary muscles was isolated from that of the rest of the LV. Dysfunction of one or both papillary muscles was produced without producing global LV dysfunction. Global LV dysfunction was also produced while keeping papillary muscle function intact. The degree of MR (assessed using contrast echocardiography) was correlated in both groups of dogs with thickening of the papillary muscles and regional and global LV function. In the group 3 dogs (n=6), the spatial distribution of blood flow within each papillary muscle was determined during ischemia by using radio labeled micro spheres. Thickening of the papillary muscles was assessed at three different levels along their lengths and was correlated with average blood flow at these levels. In group 1 dogs, MR was noted only when global LV function was affected and its severity correlated inversely with global LV function In comparison, there was poor correlation between MR and anterior and posterior papillary muscle thickening. In group 2 dogs, MR did not occur in the presence of either PMD or akinesia of the immediately adjacent LV myocardium. MR occurred only when global LV dysfunction was produced (with the papillary muscle function intact), and its severity correlated inversely with global LV function. There was poor correlation between the degree of MR and thickening of the anterior and posterior papillary muscles In both groups of dogs, MR was associated with incomplete mitral leaflet closure (IMLC), and the severity of MR correlated linearly with the degree of IMLC. MR was never associated with mitral valve prolapse. In the group 3 dogs, despite more inhomogeneous flow during ischemia to the anterior compared with the posterior papillary muscle, mean thickening of these muscles was similar (3±10% and 3±4%, respectively). Furthermore, there was minimal variability in thickening between different parts of the muscles

One year later *DR.HARI N SABBAH et al* [48] did a similar study with dog and concluded that the

shape change of left ventricle but not the simple enlargement of LV in heart failure may be an important determinant of functional MR. He examined relationship between left ventricular (LV) shape and functional mitral regurgitation (MR) was examined in 18 dogs with long-standing heart failure produced by multiple sequential intracoronary microembolisations. Global LV shape changes were evaluated from angiographic silhouettes obtained at baseline (before embolisation) and during heart failure. LV shape changes at end systole and end diastole were quantitated based upon the ratio of the major-to-minor axis and the sphericity index. Among the 18 dogs studied, 11 developed 1 + to 3+ MR during heart failure and seven did not. There was no difference among the two groups with respect to hemodynamics, LV ejection fraction, chamber volume, and regional wall motion. A significant difference, however, was observed between the two groups with respect to the global indexes of LV shape. In dogs with MR, the end-systolic major-to-minor axis ratio decreased 29 + 3% between baseline and heart failure compared with only a 18 + 3% decrease in dogs without MR ($p < 0.01$). In dogs with MR, the end-systolic sphericity index increased between baseline and heart failure compared with an increase of only 30 t 5% in dogs without MR ($p < 0.02$). Significant and directionally similar differences were observed during end diastole. These data indicate that in heart failure functional MR is associated with a more spherical LV and is not the result of simple LV chamber enlargement. Shape changes of the LV that occur in heart failure may be an important determinant of functional MR.

Few years later, *DR.SIN F YIU et al* [49] in 2000, studied the Determinants of the Degree of Functional Mitral Regurgitation in Patients With Systolic Left Ventricular Dysfunction and concluded that The presence and degree of FMR complicating LVD are unrelated to the severity of LVD. Local LV remodeling (apical and posterior displacement of papillary muscles) leads to excess valvular tenting independent of global LV remodeling. In turn, excess tenting and loss of systolic annular contraction are associated with larger EROs. These determinants of FMR warrant consideration for specific approaches to the treatment of FMR complicating LVD. In his study cohort consisted of 21 control subjects and 128 patients with LVD (defined as ejection fraction,50%, mean 31.69%) in sinus

rhythm, they quantified simultaneously by echocardiography the effective regurgitant orifice (ERO) of FMR by using 2 methods: mitral deformation (valve and annulus) and left ventricular (LV) global (volumes, stress, function, and sphericity) and local (papillary muscle displacements and regional wall motion index) remodeling. A wide range of ERO was observed, unrelated to ejection fraction The major determinant of ERO was mitral deformation, ie, systolic valvular tenting and annular contraction, independent of global LV remodeling. Systolic valvular tenting was strongly determined by local LV alterations, particularly apical and posterior displacement of papillary muscle, with confirmation in multivariate analysis, independent of LV volumes, function, and sphericity.

In 1956 *Friedberg*[11] wrote: "Relative or functional mitral insufficiency occurs commonly as a result of pronounced dilatation of the left ventricle, due to hypertensive, coronary or aortic valvular disease, usually in association with left ventricular failure. Imperfect valvular closure under such circumstances is due to dilatation of the mitral ring and to retraction of the cusps by chordae and papillary muscles as the ventricular chamber elongates." He created the concept that MITRAL ANNULAR DILATATION causes functional mitral regurgitation.

But the first clinical study to assess the mitral annular dilatation as the cause of FMR came from *DR.BOLTWOOD et al* [12] in1983. When they sought to elucidate the mechanism of mitral regurgitation (MR) in dilated cardiomyopathy

(DCM). Quantitative two-dimensional echocardiographic examinations were performed in 27 patients, 18 with DCM (nine with MR on physical examination, nine without MR) and nine without underlying heart disease. The MR and "no MR" patients were clinically comparable. Spatial reconstructions from multiple apical cross sections were used to estimate the mitral leaflet area needed to occlude the orifice for a given mid systolic coaptation configuration (LEAF), as well as mitral annular area index, left ventricular volume, and left atrial volume. Similarly, reconstructions from parasternal short-axis views were used to estimate central chordae tendinae length and angulation. From selective parasternal views papillary muscle (PM) length and contraction and the tethering

length from the PM base to the annular plane were measured. The MR group was characterized by markedly enlarged occlusional leaflet area, striking mitral annular dilatation, and left atrial enlargement . Chordal length and angulation, PM length, contraction, and tethering length, and left ventricular volume were not significantly different in the MR vs the no MR group. Non coaptation of the mitral leaflets at their free margins was not observed in any MR patient. With the use of stepwise linear regression LEAF was determined chiefly by annular size with left ventricular size having little additional influence. Thus, DCM is associated with enlargement of the mitral anulus, which is more pronounced in those patients with MR. Based on the quantitative estimates of occlusional leaflet area, we postulate that mitral leaflet tissue can stretch somewhat to accommodate dilatation of the mitral complex, but as the requirement for occlusional leaflet area increases less tissue is available for coaptation. Thus, although coaptation continues to occur, the valvular seal becomes ineffective once a critical LEAF is reached. The chief determinant of LEAF is the mitral annular size, while left ventricular size is a less important factor.

One decade later BOLTWOOD was supported by *DR SHENGQIN HE et al* [13] in 1997. He analyzed factors like annular size, position of papillary muscle, and tethering of mitral leaflet by in vitro model with excised porcine value. He concluded that annular dilatation increases regurgitation for any position of PM and creating clinically significant MR.

In contrary to above studies *DR.YATAKA OTSUJI* [14] et al in 2002 said that Isolated Annular Dilation Does Not Usually Cause Important Functional Mitral Regurgitation. In three groups of patients, 18 control subjects, 25 patients with lone AF and 24 patients with idiopathic or ischemic cardiomyopathy (ICM), for Mid-systolic MA area, MR fraction, LV volumes and papillary muscle (PM) leaflet tethering length were compared by echocardiography among. Patients with lone AF had a normal LV size and function, but MA dilation (isolated MA dilation) significant and comparable to that of patients with ICM However, patients with lone AF had only modest MR, compared with that of

patients with ICM. Multivariate analysis identified PM tethering length, not MA dilation, as an independent primary contributor to MR. He concluded that Isolated annular dilation does not usually cause moderate or severe MR. Important functional MR also depends on LV dilation and dysfunction, leading to an altered force balance on the leaflets, which impairs coaptation. This view is also supported by *Zhu et al* [50] in his study of Mechanism of Persistent Ischemic Mitral Regurgitation After Annuloplasty: Importance of Augmented Posterior Mitral Leaflet Tethering.

In all studies, whatever the controversies exists regarding the mechanisms of functional mitral Regurgitation, the only consistent proved mechanism of IMR is the **mitral leaflet tethering distance.** Two basic force act on the mitral leaflets and play important role in IMR. Ischemic LV distortion leads to papillary muscle displacement pulling the leaflet away from mitral apparatus preventing coaptation. This force is opposed by second force i.e. LV contractility tending to close the mitral leaflet. In addition to these forces papillary muscle exerts its force during systole in such way that the mitral leaflet neither prolapse nor tents to produce mitral regurgitation. Coordination of these forces requires for normal closure and coaptation of mitral valve. Defect in any of the force can leads to mitral leaflet tethering which results in functional mitral regurgitation.

In 1981 *ROBERT W. GODLEY, M.D., et a*l [51] evaluated a possible association of PM function and tethering of mitral leaflet, he performed

echocardiographic examinations on 22 patients with prior myocardial infarction and clinical evidence of papillary muscle dysfunction, 40 patients with prior myocardial infarction and no clinical evidence of papillary muscle dysfunction, and 20 normal subjects. There was a unique pattern of incomplete mitral leaflet closure in a high percentage (91%) of infarct patients with mitral regurgitation. In these patients, one or both leaflets were effectively arrested within the cavity of the left ventricle during ventricular systole. Dyskinetic wall motion in the region immediately surrounding one of the papillary muscles was present in 23 of 24 patients (96%) with demonstrated incomplete closure. This study

provides the first objective evidence that de novo

mitral regurgitation in patients with prior myocardial infarction is due to dyskinesis involving the left ventricular myocardium beneath one of the papillary muscles, producing increased tension on the mitral leaflets and preventing normal closure by increased mitral leaflet tethering distance This mechanism is supported by several investigators. Several surgical techniques were developed based on this mechanism. Mitral leaflet tethering is the primary mechanism of Recurrent mitral regurgitation after anuloplasty for functional ischemic mitral regurgitation. *Fang Zhu, MD et al* [52] hypothesized that surgical annuloplasty for ischemic mitral regurgitation (MR) that displaces the posterior annulus anteriorly can potentially augment posterior leaflet (PML) tethering, leading to persistent MR.

Relationships between leaflet configurations and persistent ischemic MR after the annuloplasty were investigated. In 31 patients with surgical annuloplasty for ischemic MR and 20 controls, posterior and apical displacement of the leaflet coaptation, the anterior leaflet (AML) and PML tethering angles relative to the line connecting annuli, coaptation length (CL), and the MR grade were quantified before and early after surgery in echocardiographic left ventricular long-axis views. Six of the 31 patients showed persistent MR despite annuloplasty. Compared with patients without persistent MR, those with MR showed no improvement in the left ventricular ejection fraction and systolic volume, similar reduction in the annular area, significant increase in posterior displacement of the coaptation , no improvement in AML tethering, greater worsening in PML tethering, and no increase in the CL. All tethering variables were significantly correlated with both preoperative and postoperative MR in univariate analysis, and reduced CL was the primary independent determinant of both preoperative and postoperative MR. Although increased AML tethering was the primary determinant of the preoperative CL, increased PML tethering was the primary determinant afterward. He concluded that although tethering of both leaflets is the major determinant of ischemic MR before surgical annuloplasty, both leaflets tethering but with predominant and augmented PML tethering is related to persistent ischemic MR after the annnuloplasty.. For Ischemic mitral regurgitation,

intraventricular papillary muscle imbrication without ring during left ventricular restoration was described in . J Thorac Cardiovasc Surg 2002. Surgical relocation of the posterior papillary muscle in chronic ischemic mitral regurgitation as one method of treatment for IMR was described in Ann Thorac Surg 2006[52].

Emmanuel Messas, MD, et al [28] in 2001 did an experiment and proposed that Chordal Cutting as a New Therapeutic Approach for Ischemic Mitral Regurgitation. It was tested in 8 mitral valves: a porcine in vitro pilot with Papillary muscle displacement and 7 sheep with acute inferobasal infarcts studied in vivo with three-dimensional (3D) echo to quantify MR in relation to 3D valve geometry. In all 8 valves, PM displacement restricted leaflet closure, with anterior leaflet angulation at the basal chord insertion, and mild-to-moderate MR. Cutting the 2 central basal chordae reversed this without prolapse. In vivo, MR increased after infarction and then decreased with chordal cutting ; this paralleled changes in the 3D leaflet area required to cover the orifice as dictated by chordal tethering. He concluded that Cutting a minimum number of basal chordae can improve coaptation and reduce ischemic MR. Such an approach also suggests the potential for future minimally invasive implementation.

ROLE OF PAPILLARY MUSCLE FUNCTION IN IMR:

Earlier in 1968 *BURCH et al* [25] discussed 'syndrome of papillary muscle dysfunction' and the contribution of papillary muscle dysfunction to the pathogenesis of ischemic mitral regurgitation and proved it by necropsy study. There was no objective evidence for that mechanism. Afterwards several studies were conducted, both experimental and in vivo, to prove the role of PM dysfunction in IMR.

In contrary to previous studies, in 1991 *DR.SANJIVE KAUL et al*,[47] did an experimental work with dogs and concluded that PMD and/or dysfunction of the immediately adjacent LV myocardium do not result in IMR.

DOES THE PAPILLARY MUSCLE FUNCTION DECREASE IMR?

Emmanuel Messas, MD et al [53] did an experimental study in sheep with the hypothesis that PM contractile dysfunction can actually diminish MR due to ischemic distortion of the inferior base alone. He occluded the proximal circumflex circulation in 7 sheep while maintaining Papillary muscle perfusion, confirmed by contrast echocardiography. By 3D echocardiography, He measured the tethering distance between the ischemic medial PM tip and anterior annulus and LV ejection volume to give MR . In 6 sheep without initial MR, inferior ischemia alone produced PM tip retraction with restricted leaflet closure and mild-to-moderate MR. Adding PM ischemia consistently decreased MR and tethering distance, as PM strain rate decreased and leaflet tenting decreased. In one sheep, prolapse and MR resolved with inferior ischemia and recurred with PM ischemia. He concluded that PM contractile dysfunction can paradoxically decrease MR from infero basal ischemia by reducing leaflet tethering to improve coaptation. This emphasizes the role of geometric factors in ischemic MR mechanism and potential therapy.

In 2005 *Takeshi Uemura, MD et al* [54] did a study to test whether papillary muscle (PM) dysfunction attenuates ischemic mitral regurgitation (IMR) in patients with left ventricular (LV) remodeling of a similar location and extent In 40 patients with a previous inferior myocardial infarction but without other lesions, the LV volume, LV sphericity, PM tethering distance, PM longitudinal systolic strain, and MR fraction were quantified by echocardiography. The patients were divided into two groups: group 1 with significant basal inferoposterior LV bulging but without advanced LV bulging involving other territories, therefore with a similar location and extent of LV remodeling, and group2 without significant LV bulging. The medial PM tethering distance was significantly correlated with the percentage of MR fraction and multiple regression analysis identified an increase in the tethering distance as the only independent determinant of the MR fraction in all subjects and also in group 1. The PM longitudinal systolic strain had no significant relationships with

MR fraction in all subjects with variable degrees of LV remodeling, but it had a significant inverse correlation with the MR fraction with LV remodeling of a similar location and extent, indicating that PM dysfunction is associated with less MR. Papillary muscle dysfunction, reducing its longitudinal contraction to induce leaflet tethering, attenuates ischemic MR in patients with basal inferior LV remodeling. (J Am Coll Cardiol 2005; 46:113–9)

On summary we have evidence for and against different mechanism of ischemic mitral regurgitation. They are left ventricular dysfunction, mitral annular dilatation, mitral leaflet tethering, dysfunction of LV myocardium and papillary muscle.

Regarding papillary muscle dysfunction as a cause of ischemic mitral regurgitation, hypothesized theories are

1. **PM dysfunction may cause IMR.**
2. **IMR may not related to PM dysfunction**
3. **PM dysfunction can attenuate IMR in some cases.**

ECHOCADIOGRAPHIC EVALUATION OF PM FUNCTION

Evaluation of papillary muscle function by any method is one of the difficult task in cardiology. Echocardiogram of papillary muscle evaluated from M mode through 2D Echo to tissue Doppler echocardiogram.

In 1972 *Tallury, DePaspuale, and Burch et al* [55] evaluated papillary muscle function in myocardial infarction patients indirectly from M Mode echocardiogram of Mitral Valve. Serial echocardiograms were recorded in 25 patients with acute myocardial infarction. Significant variations in the diastolic slope as well as in the amplitude of the mitral valve echocardiogram were found in six patients (24 per cent). An apical systolic murmur was audible in each of the six patients. Day-to-day variations in the degree of the diastolic slope as well as in the intensity of the apical systolic murmur were attributed to alterations in the dynamic (contractile) state of the papillary muscles. Thus, during

the early stages of acute myocardial infarction, ischemia and/or infarction of a papillary muscle render the muscle partially or totally incapable of shortening. Failure of the muscle to shorten results in mitral regurgitation. The echocardiogram offers a safe and convenient method for studying the day-to-day variations in papillary muscle function Cross-sectional echocardiographic spectrum of papillary muscle dysfunction study was done by *Burch, G. E., DePasquale, N. P., and Phillips, J. H. et al* [56] in 1979.

Cross-sectional echocardiography identified two abnormal patterns of mitral valve closure in 14 patients with mitral regurgitation due to papillary muscle dysfunction:

(1) in three patients with an akinetic inferior-posterior wall but normal cavity size, papillary muscle fibrosis was associated with late systolic mitral valve prolapse, and

(2) in nine patients with ventricular dilatation or ventricular aneurysm, the point of mitral valve coaptation was displaced towards the apex of the left ventricle. In two of these patients both abnormalities were observed. In contrast, abnormal patterns were identified in only four of a group of 40 patients without angiographic evidence of mitral regurgitation (10, normal; 27, coronary artery disease; three, congestive cardiomyopathy). Thus, cross- sectional echocardiography can be useful to identify mitral regurgitation secondary to papillary muscle dysfunction. Strain and strain rate echocardiography is an emerging technique for assessing myocardial systolic and diastolic function. It is envisioned that this modality could change the quantitative assessment of regional wall motion and improve the accuracy and reproducibility of test readings. Myocardial strain and strain rate can detect inducible ischemia and at earlier stages than visual estimation of wall motion or wall thickening parameters. Changes in systolic strain rate and strain have potential to discriminate between different myocardial viability states. Measurement of diastolic rate of deformation can differentiate physiologic from pathologic hypertrophy, and restrictive from constrictive cardiomyopathy. This study reviews basic principles and current experimental and clinical applications of strain and strain rate echocardiography[57].

In 2005, *Soo-Jin Kang, MD, et al* sought to assess the relationship between infarct status and systolic contractile function of papillary muscle (PM) for patients with inferior wall myocardial infarction (MI) by TDI. Peak systolic velocity of posteromedial PM, systolic strain of posteromedial PM, Peak systolic velocity of adjacent inferior wall, and systolic strain of adjacent inferior wall were calculated from color Doppler tissue imaging images obtained at apical views in 25 patients with inferior MI and in 13 healthy control subjects. All 25 patients with MI underwent magnetic resonance imaging to assess the infarct status of PM. Compared with the control subjects, patients with MI had significantly lower Peak systolic velocity of adjacent inferior wall and Peak systolic velocity of posteromedial PM and less systolic deformation, as demonstrated by less systolic strain . There was a weak positive correlation between systolic strain of inferior wall and PM for patients with MI. Magnetic resonance imaging showed total infarct of PM in 14 patients , with the remaining 11 revealing either normal perfusion or partial infarct of PM . Although systolic strain of inferior wall was similar in groups , systolic strain PM was significantly lower in with PM infract. In patients with inferior wall MI, infarct status of the PM is variable and determines its systolic contractile function, which can be quantified by systolic strain measurement using Doppler tissue imaging.[58]

THE AIM OF THE STUDY:

1) To assess the mechanisms of ischemic mitral regurgitation in patients with old myocardial infarction.

2) To assess the role of Tissue Doppler imaging in evaluation of papillary muscle function.

3) To assess the contribution of papillary muscle dysfunction in the pathogenesis of ischemic mitral regurgitation.

MATERIALS AND METHODS

This was a prospectus study done between January 2006 and January 2007 at the department of cardiology, Government General Hospital Chennai. The study cohort comprises 30 consecutive patients with old myocardial infarction and Mitral regurgitation who were referred to our department for evaluation or follow up. This study patients are divided into two groups according to location of Myocardial Infarction. Group 1 has old inferior wall myocardial infarction and Group 2 has old anterior wall myocardial infarction. Group I patients are further subdivided into 2 groups based on their left ventricular spherecity. Patients with increased left ventricular spherecity belong to Group Ia. and with normal left ventricular spherecity belongs to Group Ib. Patients are belonging to the age group of 30 – 60 years.

INCLUSION CRITERIA

1) presence of old myocardial infarction

2) Presence of Mitral regurgitation (Mild – Severe)

(Old Myocardial infarction is defined by the following character

1) History of myocardial infarction

2) ECG evidence of old MI

3) RWMA in echo

4) Elevation of cardiac enzymes at the time of Acute Myocardial Infarction)

EXCLUSION CRITERIA

1) Acute myocardial infarction(less than 1 month)
2) Multiple MI
3) Mitral regurgitation due to other causes (RHD, IE and MVPS etc.)
4) Dilated cardiomyopathy
5) Congenital heart disease.
6) Pericardial diseases.

Informed concern was obtained from all the patients.

ECHOCARDIOGRAPHY

Echocardiographic evaluation of all patients was done using Philips iE33 machine in our Echo lab III. Standard M-Mode, Two Dimensional, Color flow and tissue Doppler echocardiography was done for all patients using conventional method. Recordings of the apical four and two chamber views, long axis and parasternal short axis views were done with special attention paid to visualize the Papillary Muscle. LV end-diastolic and end-systolic cavity areas were traced in those views, and the LV end-diastolic volume (EDV) and ejection fractions (EF) were calculated by the method of discs.

LEFT VENTRICULAR SPHERICITY

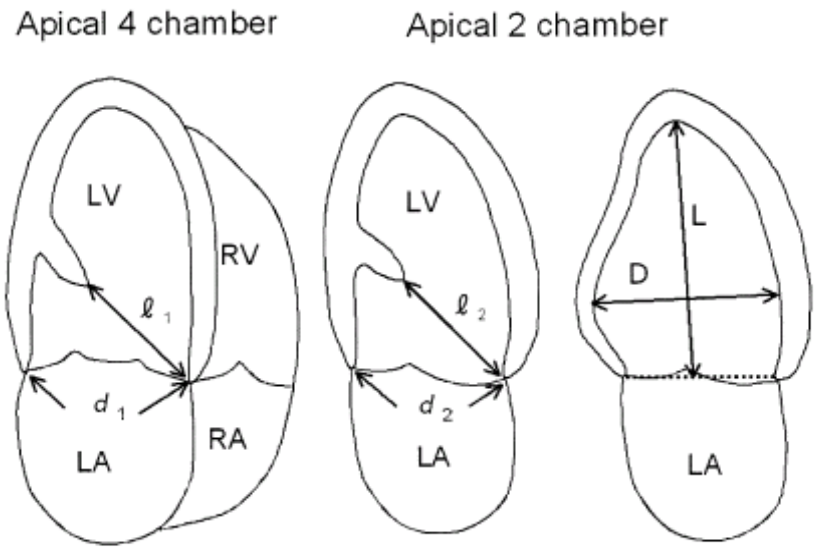
Is defined in 2 Dimensional echocardiography as ratio of short axis to long axis dimension of left ventricle. This is measured in apical two-chamber view during mid-systole. Normal value of sphericity by 2Dimensional echo method is less than 0.60. Based on the degree of basal infero-posterior LV bulging, evaluated by the short-to-long axis dimension ratio (D/L) of LV in the mid-systolic apical tow-chamber view, Group I the patients were further subdivided into two namely groups

1a with significant LV bulging with a D/L > 0.60 (upper normal value is 0.60) and group 1b without significant LV bulging with D/L < 0.60.

MITRAL ANNULAR AREA (MAA)

We assumed that the mitral annulus is elliptical in geometry during mid systole. Annular dimension of mitral valve is measured in apical 4 chamber and apical two chamber view during mid systole and mitral annular area is calculated using the formula;

$$MAA = d1 \times d2 \times \Pi/4.$$



LEAFLET TETHERING DISTANCE: [25]

As discussed in review it is the most important determinant of Ischemic mitral regurgitation .Mitral Leaflet Tethering Distance of AML and PML are measured separately. PML tethering distance is the distance between tip of PML to the controlateral anterior mitral annulus. AML tethering distance is the distance between tip of AML to the controlateral posterior mitral annulus. Both the tethering distance is measured in apical 4C and 2C views during mid

systole.

MITRAL REGURGITATION:

Is diagnosed and assessed by color flow and CW Doppler echocardiography. In our study Mitral regurgitation severity is assessed by the following methods

1) Jet Area
2) Density of CW Doppler.
3) Vena Contracta
4) Mitral Regurgitation Volume.

The jet area of MR flow is compared with area of Left Atrium and graded as mild MR if occupied less than 20% of LA. Severe MR is diagnosed if jet area occupied more than 40% of LA. Color flow Doppler signal density is compared with forward flow signal density of mitral valve. If the regurgitant flow signal density is denser than forward flow signal MR is graded as severe. Vena cotracta is the narrowest portion of MR jet and gives good correlation with severity of MR. Size of the vena contracta is > 0.7cm indicates severe MR. Mitral stroke volume was calculated as the product of the time velocity integral of transmitral flow and cross sectional area of mitral annulus. Aortic stroke volume was calculated as the product of the time velocity integral of transaortic flow and cross sectional area of left ventricular outflow. Regurgitant volume is measured by subtracting aortic stroke volume from mitral stroke volume. Regurgitant volume is >60ml indicates severe MR.

EVALUATION OF PAPILLARY MUSCLE FUNCTION

Papillary muscle systolic contraction generates tension in the chordae to maintain the systolic leaflet position and to prevent leaflet prolepses while the wall between the PM and mitral annulus contracts. Papillary muscle systolic PM contraction is spatially and temporally heterogeneous . Therefore PM dysfunction was assessed by peak systolic PM shortening in its long-axis direction or

peak systolic PM thickening in its short-axis direction.

In our study, Three methods were used to evaluate PM function [55,56]

1) M Mode Echocardiography
2) 2 Dimension Echocardiography
3) Tissue Doppler Imaging.

M-MODE ECHOCARDIOGRAPHY;

M mode echocardiography of PM is done in either apical 2C view or short axis view whichever view gives good resolution of PM and ultrasound beam perpendicular to PM. Systolic thickening of PM was measured with reference to ECG gating/ septal or posterior wall thickening.

TWO DIMENSIONAL ECHOCARDIOGRAPHY:

During two Dimensional echocardigraphic evaluations, scared and dysfunctional PM is identified by its increased echogenesity. Short axis thickening of papillary muscle during systole is measured in apical 2C or 4C view after marking the mid portion of PM muscle as reference point for measurement. Papillary muscle diameter was measured during end - systole and end – diastole at the level of reference point. End – systole is defined both by peak of T wave in ECG and begning of opening of mitral valve. End – diastole is defined both by peak of R wave in ECG and end of closure of mitral valve. Systolic thickening of papillary muscle is measured in the same way as free wall Systolic thickening using the following formula;

$$\frac{\text{END SYSTOLIC THICKNESS — END DIASTOLIC THICKNESS}}{\text{END DIASTOLIC THICKNESS}} \times 100$$

The normal systolic thickening of papillary muscle is ≥ 30% as the left ventricular free wall.

TISSUE DOPPLER IMAGING

Regional myocardial function is better assessed with TDI than any other method of echocardiography. Quantitative assessment is an important prerequisite for complete description of the dynamic changes that occur during ischemia .Conventional assessment of wall motion based on visual assessment is highly subjective and semi quantitative. Accurate assessment of regional contractile function is important for prognosis and management in patients with coronary artery disease. It has been demonstrated that wall thickening is a useful measure of regional function and is more precious than wall motion analysis . However the differentiation of regions with abnormal contractile function from regions with normal contractile function by planar method in patient with coronary artery disease is difficult because of wide range of thickening in normal and abnormal regions. The low temporal resolutions used in stress echocardiographic studies together with the limited ability of human vision to discern small differences in myocardial asynchrony, do not allow an objective quantitative assessment of complex wall motion. Tissue Doppler velocity and SRI can accurately quantify Local mechanical function with higher temporal accuracy than any current clinical method. Two dimensional strain analyses is more accurate than wall thickening analysis in discriminating dysfunctional from functional myocardium and therefore it improves the detection of regional difference in function. Two dimensional tissue Doppler and strain Doppler echocardiographic techniques used in this study allowed processing of simultaneous velocity and strain traces from apical two chamber view in the same cine loop. The Doppler ultrasonic beam was placed in mid inferior region of inferior wall of left ventricle and mid point of both papillary muscles. The Doppler ultrasonic beam was also placed in the anterior septum of left ventricle.

In our study, the systolic peak velocity, early diastolic and late diastolic peak velocity of anterior papillary muscle (APM), posterior papillary muscle (PPM), anterior septum and inferior wall are assessed in tissue Doppler study. Tissue Doppler study of papillary muscle were done in apical 4C

view or apical long axis view whichever view give good resolution of papillary muscle and ultrasound beam perpendicular to papillary muscle. Left ventricular anterior and inferior wall tissue Doppler study was done in apical 4C view or apical 2C views.

RESULTS

The study population included patient with old inferior wall and anterior wall MI complicated by mitral regurgitation. The patients were grouped into 3 groups. Group 1 patients with old inferior wall MI complicated by mitral regurgitation. These patients were further subdivided into two groups based on left ventricular sphericity as group 1a are patients with increased left ventricular sphericity and group 1b patients were with normal left ventricular sphericity. Group 2 patients are with old anterior wall MI complicated by MR..

The Demographic characteristics of patients are detailed in table 1. The average age is 49 $\pm$1 year in all groups. No significant different in gender, age and BMI in all the three groups. The distribution of coronary risk factor such as systemic hypertension, diabetes mellitus, smoking and dyslipidemia were almost equal in all the groups .The average time since Acute MI in all groups was 4 to 5 months

TABLE – 1

PATIENT PROFILE

S.No	Character	Group I a	Group I b	Group II	Pvar
1.	Age(years)	49.0	49.7	48.5	Ns
2.	Male	60%	50%	70%	Ns
3.	BMI	27$\pm$0.9	25$\pm$1.2	29$\pm$ 0.8	Ns
4.	Time since AMI	4.6mon	4.3mon	4.9mon	Ns
5.	HT	50%	50%	50%	Ns
6.	DM	60%	50%	60%	Ns
7.	Smoking	30%	30%	30%	Ns
8.	Dyslipidemia	20%	30%	50%	Ns

{BMI – Body mass index}

TABLE II

ECHO CHARACTERS OF PATIENT.

	I a	**I b**	**II**
LVFF	47.1%	54.1%	44.9%
MR (Mild)	50%	80%	60%
MR (Mod-severe)	50%	20%	40%
LV sphericity	66.0%	49.1%	58.2%
MAA	4.2cm^2	3.81 cm^2	4.44 cm^2
leaflet tethering distance			
AML tethering distance	16.7mm	17.4 mm	20.5 mm
PML tethering distance	21.6 mm	18.3 mm	16.8 mm
PM Systolic thickening			
M mode			
APM	38.7%	37.1%	30.9%
PPM	31.8%	31.0%	41.5%
2D ECHO			
APM	36.7%	33.7%	27.5%
PPM	31.6%	32.3%	32.4%
Systolic peak velocity in TDI			
APM	7.35 m/s	7.36 m/s	6.73 m/s
PPM	6.90 m/s	6.40 m/s	7.68 m/s

{LVEF – left ventricular ejection fraction;MR- mitral regurgitation;MAA-Mitral annular area;AML-Anterior mitral leaflet;PML-Poterior mitral leaflet;APM-Anterio lateral papillary muscle; PPM-Posterio medial papillary muscle; TDI- Tissue Doppler imaging;}

The echocardiographic characters of the patient are listed in table II. .The average left ventricular ejection fraction is higher in group Ib compared to group Ia and II (54.1%vs47.1%&44.9% $p<0.01$).This can be explained by low incidence of moderate MR and normal left ventricular sphericity in group I b .The incidence of moderate to severe mitral regurgitation is high in group Ia and II compared to Ib (50%and 40%vs. 20% $p<0.01$)

The average left ventricular sphericity is high in group Ia compared to group Ib & groupII (66%VS 49.1%&58.2%).The mitral annular area is higher in both group Ia&II compared to group Ib (42mm&44mmVS 38mm $p>1$)which is not statistically significant We will compare the leaflet tethering distance of PPM in inferior wall MI and APM in anterior wall MI. .The average leaflet

tethering distance of PPM is high in Ia compared to group Ib (21.6VS18.3mm).The average tethering distance of AML is 20.5mm in group II .Systolic thickening of and PPM and APM were compared in M MODE and 2D echo, the average systolic thickening of PPM in Ia and II were 31.6%&32.3%.The value for APM in group II is 27.5%.

TABLE III

TISSUE DOPPLER IMAGING

	I a	**I b**	**II**
APM			
Sm peak m/s	9.1±1.0	9.1±0.9	6.2±0.8
Em peak m/s	9.8±1.3	9.9±1.2	8.5±1.3
Am peak m/s	10.2±0.8	10.3±0.6	9.8±1.0
PPM			
Sm peak m/s	6.3±0.9	6.8±1.6	8.2±1.6
Em peak m/s	9.8±1.3	9.0±1.2	9.2±1.2
Am peak m/s	10.2±0.8	9.8±0.8	9.8±2.26
Anterior septum			
Sm peak m/s	8.7± 0.8	8.9±0.7	5.2±0.2
Em peak m/s	9.8±1.3	9.9±1.2	8.5±1.3
Am peak m/s	10.2±0.8	10.3±0.6	9.8±1.0
Inferior wall			
Sm peak m/s	5.5±0.4	5.7±0.2	8.8±1.0
Em peak m/s	9.8±1.3	9.0±1.2	9.2±1.2
Am peak m/s	10.2±0.8	9.8±0.8	9.8±2.26

{ APM-Anterior papillary muscle; PPM-Posterior papillary muscle; TDI- Tissue Doppler imaging; Sm-systolic peak velocity, Em-early diastolic peak velocity Am-atrial peak velocity }

The results of Doppler echocardiography analysis are reported in table III. Peak systolic velocity, early diastolic and late atrial diastolic velocity of anterior septum, posterior wall and both papillary muscle were recorded. As expected the systolic peak velocity of inferior wall is reduced in both group Ia and Ib (5.5 ± 0.4 &5.7±0.8) compared to anterior wall MI (8.8±1). Similarly The peak systolic velocity of anterior wall is reduced in group II as compared to group I (5.2±0.2)vs. (8.7±0.8).The peak systolic velocity of posterior papillary muscle in group Ia and Ib are 6.9 and 6.4 m/s where in group II is 7.68 m/s . The APM systolic peak velocity in group II is 6.73 m/s compared to

group I(7.35 m/s)

TABLE IV

DETERMINANT OF ISCHEMIC MR

	I a	**I b**	**II**
LV Sphericity	66.0%	49.1%	58.2%
Mitral Annular Area	4.24 cm	3.81 cm	4.44 cm
Leaflet Tethering Distance			
AML	16.7 mm	17.4 mm	20.5 mm
PML	21.6 mm	18.3 mm	16.8 mm
Papillary Muscle Peak Velocity			
PPM	6.90m/s	6.40m/s	7.68m/s
APM	7.35m/s	7.36m/s	6.73m/s
PM systolic thickening			
APM	38.7%	37.1%	30.9%
PPM	31.8%	31.0%	41.5%

The determinants of ischemic mitral regurgitation namely LV sphericity, MAA, leaflet tethering distance and papillary muscle function are analysed in tableIV.The LV sphericity is higher in group Ia than group Ib and II(66% vs. 49.1% and 58.2%) .Mitral annular area does not show significant difference in all the groups. Posterior leaflet tethering distance is higher in group I whereas anterior leaflet tethering distance is higher in group II. Posterior papillary muscle peak velocity is lower in group I where as anterior muscle is lower in group II (6.4m/s vs.6.73m/s) as systolic thickening of corresponding papillary muscle.

TABLE V

COMPARISON OF DETERMINANT OF ISCHEMIC MR

Sl.	**Catachrestic**	**Mild MR**	**Mod –severe**	**P value**

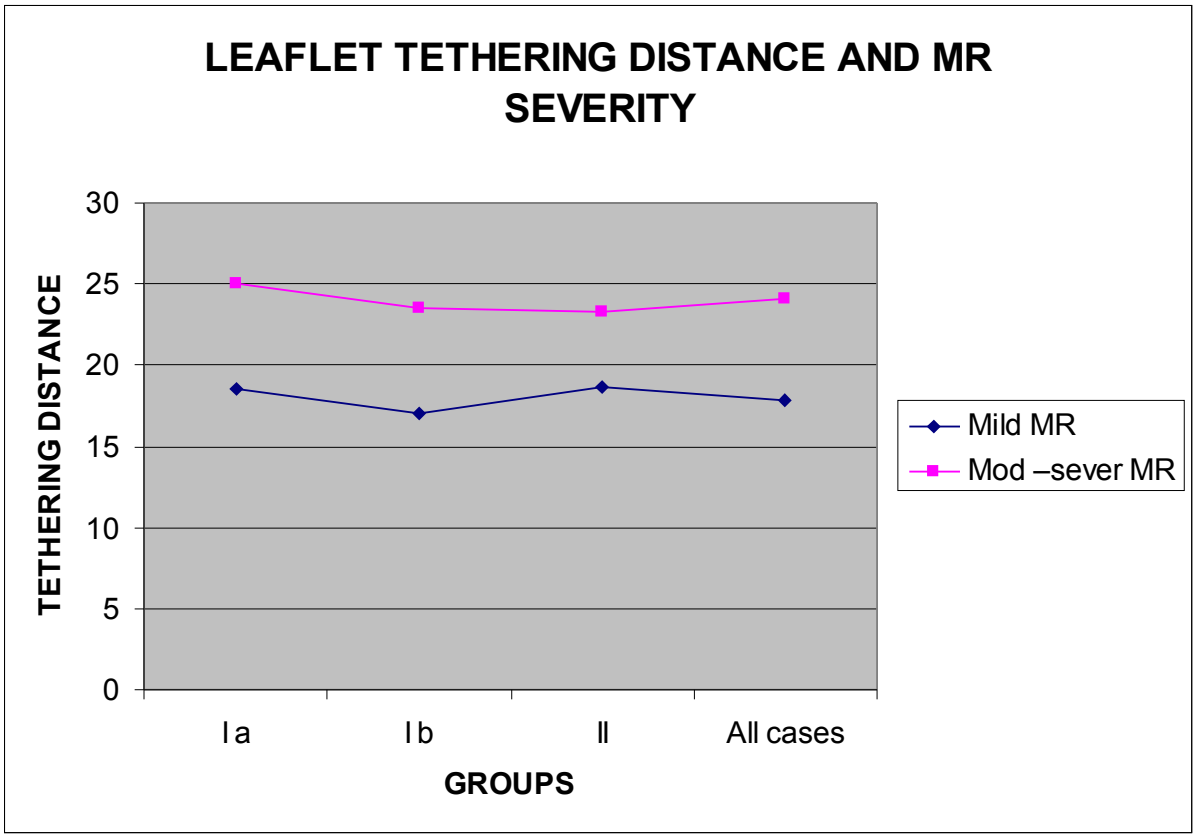
No			MR	
1.	LV sherecity			
	I a	63.00%	69.00%	<0.01
	I b	48.25%	52.50%	ns
	II	55.50%	55.50%	ns
	All cases	50.90%	52.50%	ns
2	Mitral Annular Area			
	I a	38.4mm	46.4 mm	<0.05
	I b	38.5 mm	38.5 mm	ns
	II	48.5 mm	51.5 mm	ns
	All cases	41.2 mm	46.8 mm	<0.01
3	Leaflet tethering Distance			
	I a	18.50 mm	25.00 mm	<0.01
	I b	17.00 mm	23.50 mm	<0.05
	II	18.60 mm	23.25 mm	<0.05
	All cases	17.84 mm	24.09 mm	0.01
4	**PM function**			
	Systolic Velocity			
	I a(PPM)	5.98 m/s	7.90 m/s	<0.05
	I b(PPM)	7.41 m/s	7.10 m/s	ns
	II(APM)	7.06 m/s	6.35 m/s	ns
	Systolic thickening			
	I a(PPM)	24%	40%	<0.05
	I b(PPM)	36%	33%	ns
	II(APM)	30%	29%	ns

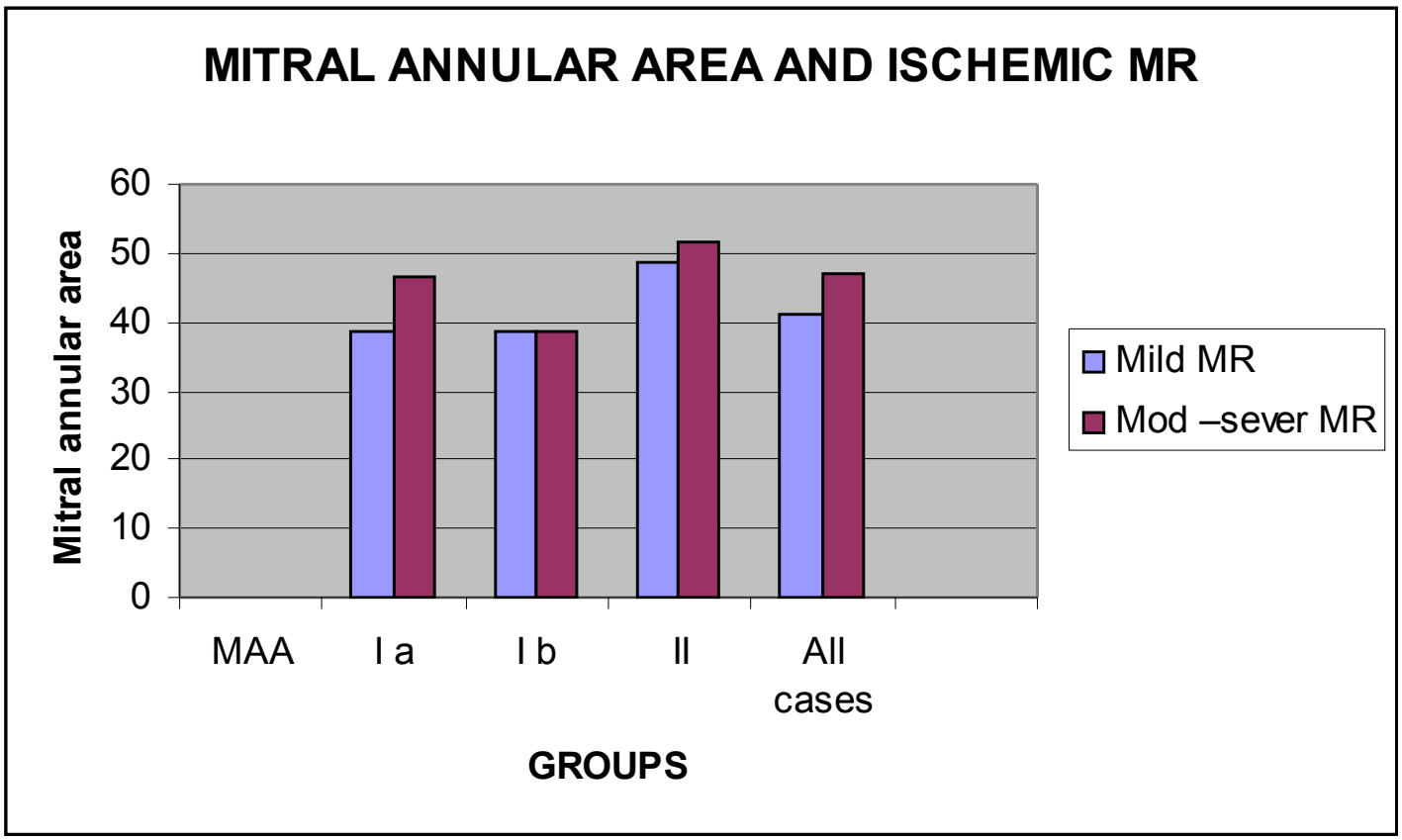
(MAA-Mitral annular area; AML-Anterior mitral leaflet; PML- Posterior mitral leaflet; APM-Anteriolateral papillary muscle; PPM- Posteriomedial papillary muscle; TDI- Tissue Doppler imaging;}

RESULT ANALYSIS

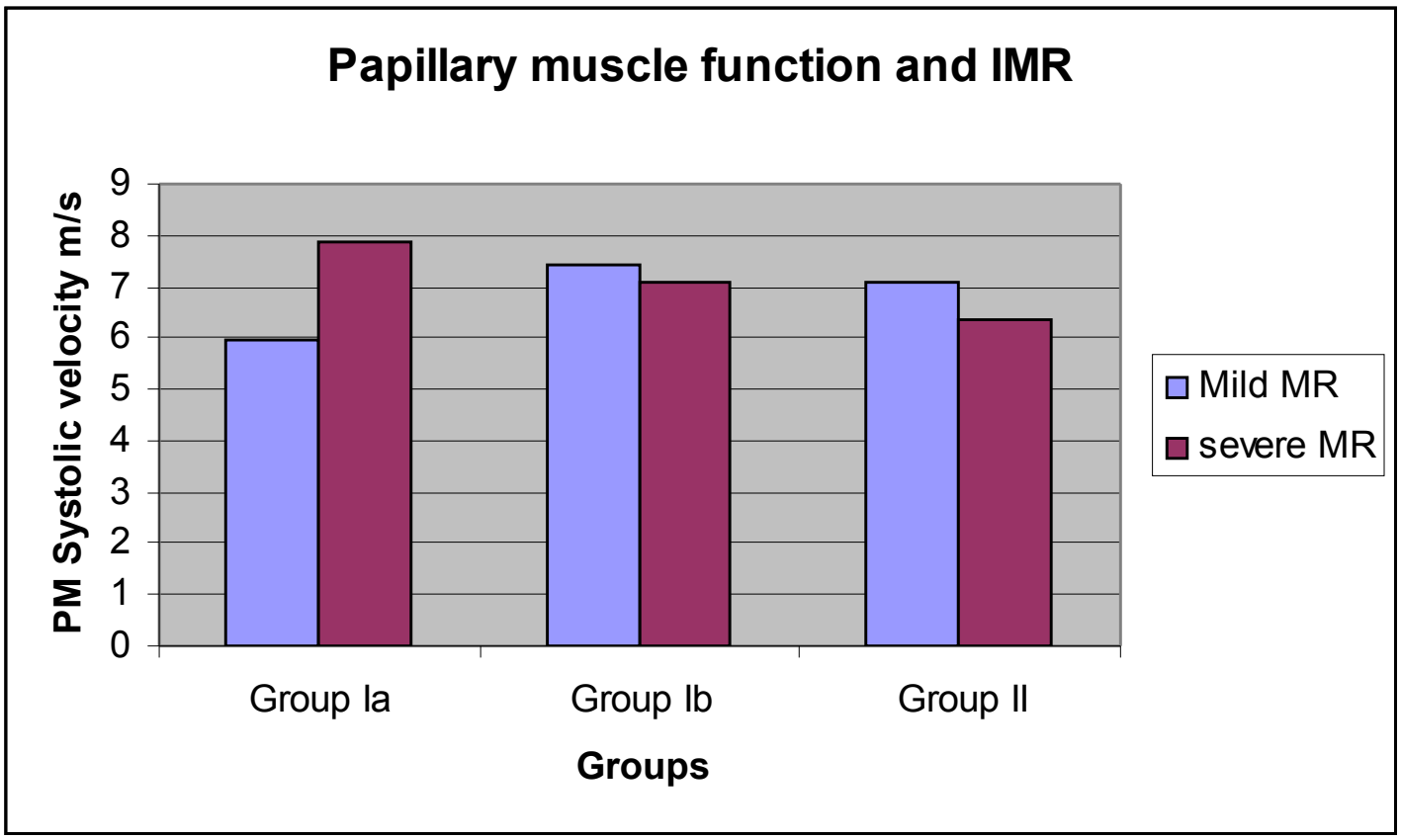
This line diagram clearly demonstrates the linear relationship of leaflet tethering distance and severity of ischemic mitral regurgitation. In all groups of patients when there is severe MR

the leaflet tethering distance is high.



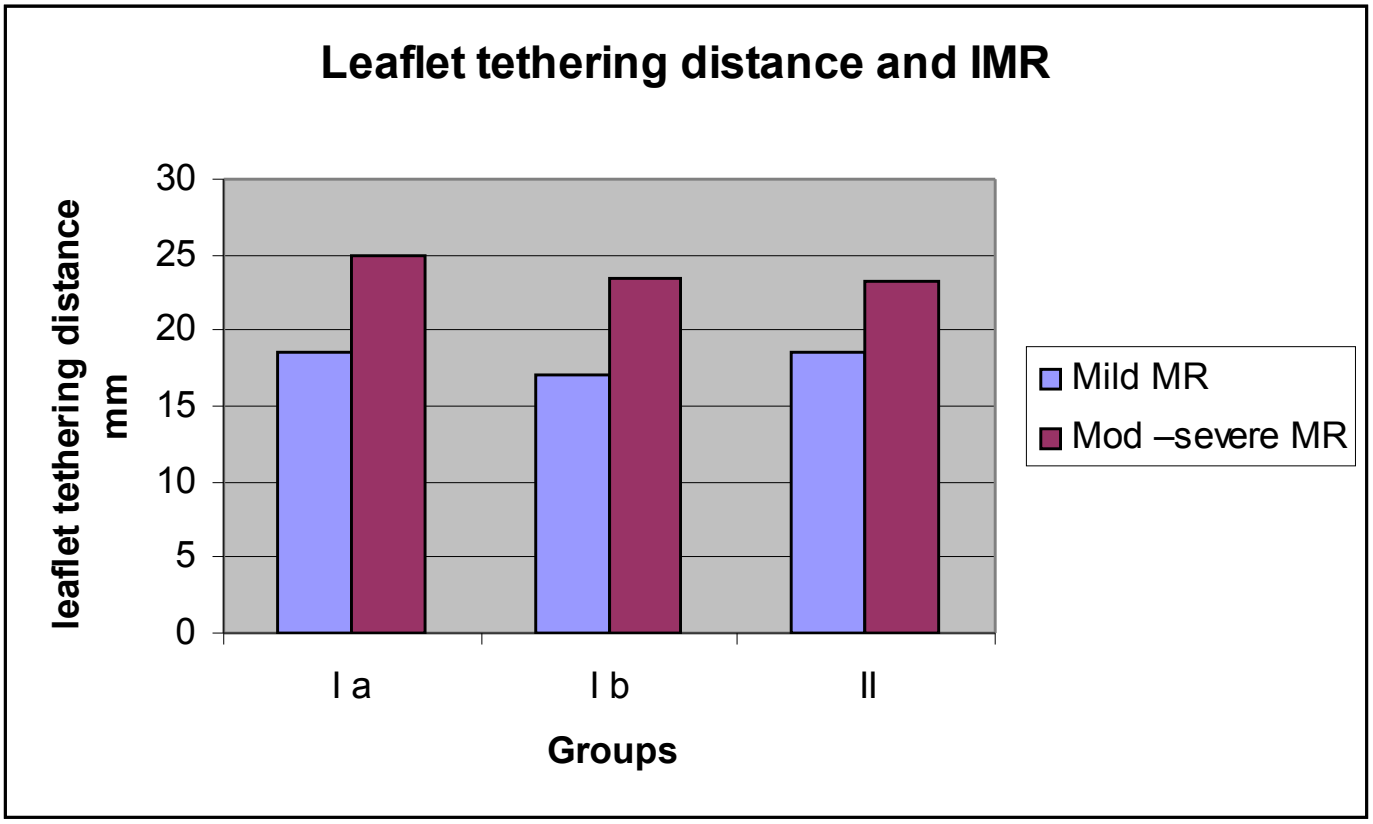


This BAR chart depicts the relationship of mitral annular area with severity of ischemic mitral regurgitation. The MAA does not have the consistent correlation with severity of MR.

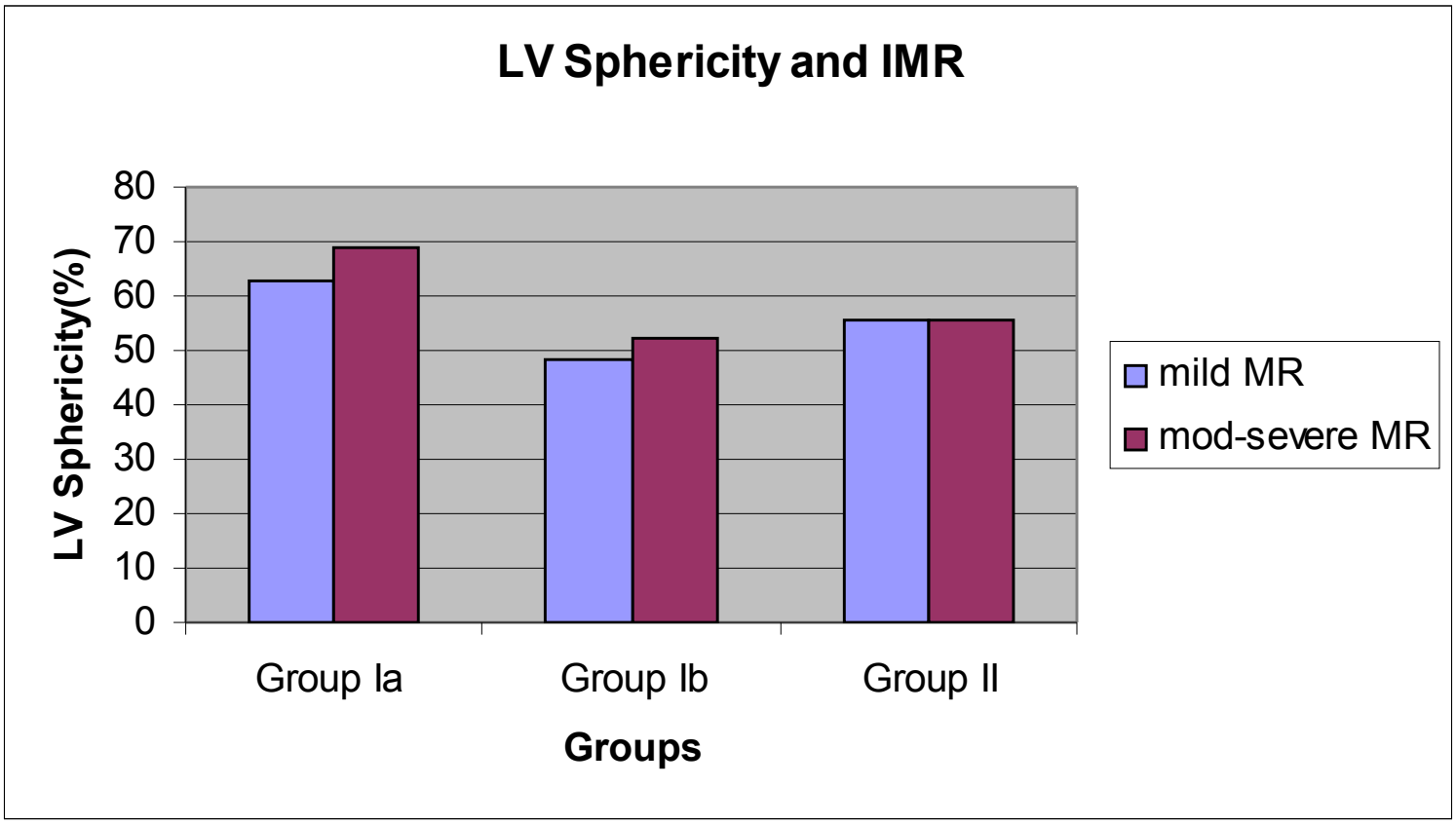


This bar diagram depicts the relationship between papillary muscle function with ischemic mitral regurgitation. The papillary muscle systolic peak velocity does not have consistent

correlation with ischemic mitral regurgitation in all groups. In group Ia papillary muscle systolic peak velocity has linear correlation with ischemic mitral regurgitation. In other words normal papillary muscle function is associated with severe MR.



This bar diagram depicts the relationship between leaflet tethering distances with ischemic mitral regurgitation. There is linear relationship between leaflet tethering distance and severity of ischemic mitral regurgitation in all group of patients..



This BAR chart depicts the relationship of LV sphericity with severity of ischemic mitral regurgitation. The LV sphericity has good correlation with severity of MR in group Ia but not in other groups.

DISCUSSION

Ischemic mitral regurgitation (IMR) is a common complication of both acute and chronic ischemic heart disease and adversely affects the prognosis by doubling the risk of death.[8,9] Since its initial recognition by *Burch and Depasquek*,[25] Ischemic MR has been attributed in both, name and mechanism, to dysfunction of papillary muscle impairing the normal support of effective cooptation with prolapse of leaflet.

However, isolated papillary muscle dysfunction failed to produce ischemic MR in animal models.[59-62] In addition mitral leaflet prolapse which can be caused by Papillary muscle dysfunction is rare in patients with ischemic MR.[63-65]

Therefore, the relationship between Papillary muscle dysfunction and ischemic MR has not been established concretely.

Prevailing explanations for such ischemic MR have focused on two factors:

(1) Ischemic distortion of left ventricular geometry, displacing the attachments of the mitral leaflets to the Papillary muscles and annulus and restricting their ability to close effectively at the annular level, [12-19] (2) Decreased left ventricular (LV)-generated force acting to close the leaflets, particularly when they are under increased tension.[18] Both factors would produce the apically tented or tethered leaflet configuration referred to as incomplete mitral leaflet closure(IMLC) Nevertheless, a potential contributory role of Papillary muscle contractile dysfunction has remained with in the range of proposed mechanisms. This persistent notion is particularly problematic when we consider the following reasoning: If, in fact, ischemic MR results from a net imbalance of apically directed forces-

increased tethering and diminished LV contraction-then normal PM contraction, which is also directed toward the apex, should in principle increase apical tethering and augment IMR. Conversely we can propose the hypothesis that in the presence of MR caused by increased tethering, for example, from ischemia with outward distortion of the inferior base of the heart (but not involving the Papillary muscles), adding contractile dysfunction of the Papillary muscles can paradoxically diminish IMR by allowing the leaflets to seat better and approach the annular level more closely to close more effectively. Tethering may also be reduced by possible stretching of the ischemic papillary muscle towards the annulus by LV force transmitted through the leaflets and chordae. Testing this hypothesis is important not only to sharpen our understanding of mechanism but also practically because abnormal tethering can potentially be addressed mechanically, but restoring Papillary muscle contractile function may not be possible.

Regional Wall Function by Echocardiography: [66,67]

An accurate value of regional myocardial function is systolic thickening (Expressed as a Percentage). Wall thickening is directly related to myocardial function and abnormalities in wall thickening are correlated to well with the extent of Infarct size. However the differentiation of regions with abnormal contractile function from regions with normal function by planer method with coronary artery disease is difficult because of wide range of thickening in normal and abnormal regions. Tissue Doppler Echocardiography velocity can accurately quantify local myocardial function with higher temporal accuracy than any current clinical method.

Papillary Muscle Function by Echocardiography:[68,69]

Evaluation of Papillary muscle function by echocardiography progressed from M mode through 2D to tissue Doppler echocardiography (TDI). As discussed previously regional myocardial function like Papillary muscle function can be clearly quantifiable by TDI than conventional 2D and M mode

echocardiography even though TDI is an angle dependent ultrasound technique and papillary muscle is small intracavitary structure. TDI is better than other conventional methods in assessing the PM function quantitatively. On the other hand left ventricular dilation by left ventricular sphericity, mitral annular area and leaflet tethering distance are also assessed and correlated with degree of IMR in our study.

Mitral Annular Area:

'Mitral annular dilatation causes functional MR' concept was created by Dr. Friedberg[11] in 1956. This concept was both supported and contradicted by different authors in the following years. In our study mitral annual area is increased in patients with moderate to severe mitral regurgitation than patients with mild mitral regurgitation (46.8mm vs. 41.2mm, $p>0.10$). However it is significant in patients with increased LV sphericity than patients with normal left ventricle sphericity index (46.4mm Vs 38.4mm $p<0.05$). But when the LV sphericity is equal mitral annular area does not correlate with severity of MR.

Left ventricular Sphericity:

Is determined by remodeling of different segments of left ventricle. Mitral valve geometry is affected greater in patients with focal LV remodeling than extensive remodeling of left ventricle. In our study the incidence of moderate to severe MR is directly proportional to left ventricular sphericity index. The incidence of MR in patients with increased LV sphericity to normal LV is 50% vs. 20% $p<0.01$. Our study results correlated well with both experimental work done by Dr. HARINSABBAHNI et al[48] and human work by Dr. SINFYIU et al[49] in 2000. In patients with moderate to severe MR the average left ventricular sphericity is 62.33% (p value <0.05) when compared to patients with mild MR is 50.90%.

Leaflet tethering distance:

In our study the most consistent factor that correlated with the severity of Ischemic mitral regurgitation is the mitral leaflet tethering distance. In all groups of patients, the leaflet tethering distance with moderate to severe MR compared to mild MR is 24.09 mm Vs. 17.84 mm [P<0.01]. Mitral leaflet tethering distance is directly proportional to the severity of MR. Our study correlated well with the result of both experimental and human studies in the past by Dr. Robert W Godley, MD, et al[51]. in 1981. Mitral leaflet tethering distance was proposed by Dr. Fang Zhu, MD et al[52] as the primary mechanism of persistent MR even after mitral Annuloplasty.

PAPILLARY MUSCLE FUNCTION:

"SYNDROME OF PAPILLARY MUSCLE DYSFUNCTON" was first described by DR GE BURCH et al [25] in 1968 and contributed to the pathogenesis of IMR. He proved the above by autopsy and indirect evidence from echo in the following years. Since the first description is the most controversial subject in cardiology is papillary muscle dysfunction and ischemic MR. In 1991 DR SANJEEVKAUR et al disproved this concept in experimental works with dogs .With advent of tissue doppler study & regional wall assessment by TDI,[66,67] the function of papillary muscle was asssesd better. In our study papillary muscle dysfunction has no linear correlation with severity of ischemic MR. Infact in patients with inferior wall MI & focal remodeling as evidenced by increased LV sphericity ,there is inverse relationship with ischemic MR and papillary muscle dysfunction .The systolic peak velocity of papillary muscle in patients in mild MR is 5.98 m/s compared to severe MR of 9.0 m/s. The systolic thickening of papillary muscle in patients with mild MR compared to severe MR were 24% vs. 40% (p<0.01).But when there is normal LV sphericity as due to no focal remodeling or uniform remodeling, there is no such correlation with the severity of IMR and papillary muscle dysfunction

CLINICAL APPLICATIONS.

The results of the study suggest a central role of leaflet tethering [59-65,] as opposed to Papillary muscle dysfunction, in the mechanism responsible for ischemic MR. Therapeutic approaches to relieve ischemic MR need to be targeted to reduce tethering by LV remodeling. Revascularization of the viable adjacent LV wall is expected to relieve ischemic MR[70]. The results also support the surgical approaches targeted at relieving tethering by aneurysm plication and repositioning of Papillary muscles [71-74.] In addition, our results suggest that the term "PM dysfunction" be changed to "PM displacement" to better describe ischemic MR.

STUDY LIMITATIONS.

Ischemic MR includes a wide spectrum of underlying pathophysiologies, such as acute or chronic and global or segmental LV remodeling [59-65]. The present study only addressed ischemic MR due to chronic inferoposterior MI, and chronic anterior wall MI and found an inverse relationship between PM dysfunction and the degree of MR in chronic inferoposterior MI,. Although PM dysfunction with reduced systolic longitudinal shortening, in theory, is expected to attenuate tethering and MR

In general patients with ischemic MR, such an inverse relationship may not be relevant in many patients with ischemic MR due to different pathophysiologies, such as dilated/ ischemic cardiomyopathy other entities with only modest variability in Papillary muscle dysfunction and more extensive LV remodeling. Medial and anterolateral Papillary muscle displacement was evaluated by determining Papillary muscle tethering length by 2D echocardiography. Because PM contraction varies according to the spatial direction,[75] it is necessary to attempt to establish a standard angle used for echocardiographic evaluation of PM systolic peak velocities and to carefully interpret the derived data.

In our study Papillary muscle function was evaluated by M Mode, 2D Echo and TDI systolic peak velocity. But the currently available best echo method to assess the regional wall is Tissues Doppler Strain rate imaging..[66,67]

CONCLUSIONS

1. Mitral leaflet tethering distance is consistently directly proportional to severity of Ischemic mitral regurgitation.
2. Papillary muscle function is better assessed by tissue Doppler echo than M Mode and 2D echocardiography.
3. Papillary muscle dysfunction is not an independent determinant of ischemic MR in all cases.
4. Papillary muscle dysfunction attenuates ischemic MR in patients with old inferior wall MI with increased left ventricular sphericity due to focal remodeling.
5. Role of papillary muscle dysfunction in ischemic MR is still elusive and varies depending on factors such as location of myocardial infarction and extent of left ventricular remodeling.

BIBLIOGRAPHY

1) Kono T, Sabbah HN, Rosman H, et al. Mechanism of functional mitral regurgitation during acute myocardial ischemia. J Am Coll Cardiol 1992; 19:1101–5.
2) Trehan,N, sharma VK; Kumar A; coronary artery bypass surgery in Indians. New devlopement in cardiology and cardiovascular surgry. Escorts Heart Instutite and Resardh centre; 159-169.
3) Birnbaum Y, Chamoun AJ, Conti VR et ai; Mitral regurgitation in acute myocardial infarction. Coron Artey Dis 13;337-344, 2002.
4) Trichon BH; Felker GM; Shaw LK et al; Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular dysfunction and heart failure. Am J Cardiol 91;538-543;2003
5) .Kumanohoso T, Otsuji Y, Yoshifuku S, et al. Mechanism of higher incidence of ischemic mitral regurgitation in patients with inferior myocardial infarction: quantitative analysis of left ventricular and mitral valve geometry in 103 patients with prior myocardial infarction. J Thorac Cardiovasc Surg 2003;125:135– 43

6) KE Fleischmann, L Goldman, PA Robiolio, RT Lee, PA Johnson, EF Cook, and TH Lee Echocardiographic correlates of survival in patients with chest painJ Am Coll Cardiol, 1994; 23:1390-1396
7) Dalen and Alpert, 2nd edition little Brown 1987, p112
8) Lamas GA, Mitchell GF, Flaker GC, et al. Clinical significance of mitral regurgitation

9 Grigioni F, Enriquez-Sarano M, Zehr KJ, Bailey KR, Tajik AJ.
after acute myocardial infarction. Survival and Ventricular Enlargement investigators. Circulation 1997;96:827–33.

10 schemic mitral regurgitation: long-term outcome and prognostic implications with quantitative Doppler assessment. Circulation 2001; 103:1759–64.

11 Godley RW, Wann LS, Rogers EW, Feigenbaum H, Weyman AE. Incomplete mitral leaflet closure in patients with papillary muscle dysfunction. Circulation 1981;63:565–71

12 Friedberg CK Diseases of heart 2 nd edition Philadelphia: WB Saunders Co, 1956:640.

13 CM Boltwood, C Tei, M Wong and PM Shah Quantitative echocardiography of the mitral complex in dilated cardiomyopathy: the mechanism of functional mitral regurgitation *Circulation* 1983;68;498-508

14 Shengqiu He, MD; Arnold A. Fontaine, PhD; Ehud Schwammenthal, MD, PhD; Ajit P. Yoganathan, PhD; ; Robert A. Levine, MD Integrated Mechanism for Functional Mitral Regurgitation Leaflet Restriction Versus Coapting Force: In Vitro Studies *Circulation.* 1997;96:1826-1834

15 Yutaka Otsuji, MD, FACC*,*, Toshiro Kumanohoso, MD*, Isolated annular dilation does not usually cause important functional mitral regurgitation
Comparison between patients with lone atrial fibrillation and those with idiopathic or ischemic cardiomyopathy J Am Coll Cardiol, 2002; 39:1651-1656

16 20 Siu F. Yiu, Maurice Enriquez-Sarano, Christophe Tribouilloy, James B. Seward, and A. Jamil Tajik Determinants of the Degree of Functional Mitral Regurgitation in Patients With Systolic Left Ventricular Dysfunction : A Quantitative Clinical Study Circulation 2000 102: 1400 – 1406

17 Dent JM; Spotnitz W D; Nolan SP et al; Mechanishm of mitral leaflet excursion Am J Physiol 1995;269:H 2100-8

17 Yutaka Otsuji, MD, FACCa, Mark D. Handschumacher, BSa, Mechanism of ischemic mitral

regurgitation with segmental left ventricular dysfunction: three-dimensional echocardiographic studies in models of acute and chronic progressive regurgitation J Am Coll Cardiol, 2001; 37:641-648

18) Nozomi Watanabe, MD, FACC, Geometric Differences of the Mitral Valve Tenting Between Anterior and Inferior Myocardial Infarction with Significant Ischemic Mitral Regurgitation: Quantitation by Novel Software System with Transthoracic Real-time Three-dimensional Echocardiography, Journal of the American Society of Echocardiography **72;** January 2006

19) Sandler H; Dodge H ; Left ventricular tension and stress in man. Circ Res 1963: 13: 91-104.

20) Yiu SF, Enriquez-Sarano M, Tribouilloy C, Seward JB, Tajik AJ.Determinants of the degree of functional mitral regurgitation in patients with systolic left ventricular dysfunction: a quantitative clinical study. Circulation 2000;102:1400–6.

21 A Kisanuki, Y Otsuji, R Kuroiwa, T Murayama Two-dimensional echocardiographic assessment of papillary muscle contractility in patients with prior myocardial infarction J Am Coll Cardiol, 1993; 21:932-938

22 Emmanuel Messas, J. Luis Guerrero, Mark D. Handschumacher, Chi-Ming Chow, Suzanne Sullivan, Ehud Schwammenthal, and Robert A. Levine Paradoxic Decrease in Ischemic Mitral Regurgitation With Papillary Muscle Dysfunction: Insights From Three- Dimensional and Contrast Echocardiography With Strain Rate Measurement Circulation 2001 104: 1952 - 1957,

23 Takeshi Uemura, Yutaka Otsuji Papillary Muscle Dysfunction Attenuates Ischemic Mitral Regurgitation in Patients With Localized Basal Inferior Left Ventricular remodeling: Insights From Tissue Doppler Strain Imaging *J. Am. Coll. Cardiol.* 2005;46;113-119

24 Estes, E. H., Jr., Dalton, F. M., Entman, M. L., Dixon, H. B., II, and Hackel, D. B.: The

anatomy and blood supply of the papillary muscles of the left ventricle, AM HEART J 71:356, 1966.

25 Burch GE, De Pasquale NP, Phillips JH. The syndrome of papillary muscle dysfunction. Am Heart J 1968;75:399–415.

26 Joseph k. perloff and william c. Roberts The Mitral Apparatus: Functional Anatomy of Mitral Regurgitation *Circulation* 1972;46;227-239

27 CHENG TO: Some new observations on the syndrome of papillary muscle dysfunction.Amer J Med 47: 924, 1969

28 MOLLER JH, LuCAs RV, ADAMS P, ANDERSON RC, JORGENS J, EDWARDS JE: Endocardial fibroelastosis. Circulation 30: 759, 1964

29 LEVY MJ, EDWARDS JE: Anatomy of mitral insufficiency. Progr Cardiovasc Dis 5: 119, 1962

30 BROLIN I: The mitral orifice. Acta Radiol Diagn 6: 273, 1967 237

31 DAVIS PKB, KINMOUTH JB: The movements of the annulus of the mitral valve. J Cardiovasc Surg 4: 427, 1963

32 SARNOFF SJ, GILMORE JP, MITCHELL JH Influence of atrial contraction and relaxation on closure of mitral valve: Observations on effects of autonomic nerve activity. Circ Res 11: 26, 1962

33 SHAH PM, KRAMER DH, GRAMIAK R: Influence of the timing of atrial systole on mitral valve closure and on the first heart sound in man. Amer J Cardiol 26: 231, 1970

34 VANDENBERG RA, WILLIAMS JCP, STURM RE, WOOD EH: Effect of varying ventricular function by extra systolic potentiation on closure of the mitral valve. Amer J Cardiol 28:43, 1971

35 EDWARDS JE, BURCHELL HB: Endocardial and intimal lesions (jet impact) as possible sites of origin of murmurs. Circulation 18: 946, 1958

36 BROCK RC: The surgical and pathological anatomy of the mitral valve.
Brit Heart J 14: 489, 1952

37 MONTIEL MN: Muscular apparatus of the mitral valve in man and its involvement in left-sided cardiac hypertrophy. Amer J Cardiol 26: 341, 1970

38 Brock, R. C.: The surgical and pathological anatomy of the mitral valve, Brit.
Heart J.14:489, 1952.

39 Chiechi, M. A., Lees, W. M., and Thompson, R.: Functional anatomy of the normal mitral valve, J. Thoracic Surg. 32:378, 19.56.

40 Rushmer, R. F., Finlayson, B. L., and Nash, A. A.: Movements of the mitral valve, Circulation Res. 4~337, 1956.

41 Davila, J. C., and Palmer, T. E.: The mitral valve, Arch. Surg. 84:174, 1962.

42 Brockman, S. K.: Mechanism of the movements of the atrioventricular valves, .4m. J. Cardiol. 17:682, 1966.

43 Burch, G. E., and DePasquale, N. P.: Time course of tension in papillary muscles of the heart, J.A.M.A. 192:701, 1965.

44 Puff, von A., Barrenberg, M., and Goerttler, T.: Rijntgenkinematographische Untersuchungen iiber den Bewegungsmechanismus der Mitralklappe,
Fortschr. Geb. RGntgenstrahlen. 102: 607, 1965.

45 Burch, G. E., Ray, C. T., and Cronvich, J. A.: The George Fahr Lecture: Certain mechanical peculiarities of the human cardiac pump in normal and diseased states,
Circulation 5:504, 1952.

46 DePasquale, N. P., and Burch, G. E.: The necropsy incidence of gross scars or acute infarction of the papillary muscles of the left ventricle, Am. J. Cardiol. 17:169, 1966.
Edwards, J. E., and Burchell, H. B.: Pathologic

47 S Kaul, WD Spotnitz, WP Glasheen and DA Touchstone ; Mechanism of ischemic mitral

regurgitation. An experimental evaluation *Circulation* 1991;84;2167-2180

48) Hani N. Sabbah, PhD, Tatsuji Kono, MD, Left ventricular shape: A factor in the etiology of functional mitral regurgitation in heart failure (AM HEART J 1992;123:981.)

49 Yiu SF, Enriquez-Sarano M, Tribouilloy C, Seward JB, Tajik AJ. Determinants of the degree of functional mitral regurgitation in patients with systolic left ventricular dysfunction: a quantitative clinical study. Circulation 2000;102:1400–6.

50 Fang Zhu, Yutaka Otsuji, Goichi Yotsumoto, Mechanism of Persistent Ischemic Mitral Regurgitation After Annuloplasty: Importance of Augmented Posterior Mitral Leaflet Tethering *Circulation* 2005;112;396-401

51 Godley RW, Wann LS, Rogers EW, Feigenbaum H, Weyman AE. Incomplete mitral leaflet closure in patients with papillary muscle dysfunction. Circulation 1981;63:565–71

52 McGee Jr EC, Gillinov AM, Blackstone EH, Rajeswaran J, Cohen G, Najam F, Shiota T, Sabik JF, Lytle BW, McCarthy PM, Cosgrove DM.Recurrent mitral regurgitation after annuloplasty for functional ischemic mitral regurgitation. *J Thorac Cardiovasc Surg.* 2004;128:916 –924.

53 Messas E, Guerrero JL, Handschumacher MD, et al. Paradoxic decrease in ischemic mitral regurgitation with papillary muscle dysfunction: insights from three-dimensional and contrast echocardiography with strain rate measurement.Circulation 2001;104:1952–7

54 Takeshi Uemura, Yutaka Otsuji Papillary Muscle Dysfunction Attenuates Ischemic Mitral Regurgitation in Patients With Localized Basal Inferior Left Ventricular remodeling: Insights From Tissue Doppler Strain Imaging *J. Am. Coll. Cardiol.* 2005;46;113-119

55) V. K. Tallury, M.D. N. P. DePasquale, M.D. G. E. Burch, M.D. New York, N. Y., and New Orleans, La. The echocardiqgram in pupikwy muscle dysfuncfion American Heart Journal January, 1972 Vol. 83, No. 1, pp. 12-18

56) Satoshi Ogawa, M.D. Francis E. Hubbard, M.D. T. Joseph Mardelli, M.D. Leonard S. Dreifus, M.D. Cross-sectional echocardiographic spectrum
of papillary muscle dysfunction American Heart Journal March, 1979, VoE. 97, No. 3

57) Cristina Pislaru, MD, Theodore P. Abraham, MD and Marek Belohlavek, MD, PhD Strain and strain rate echocardiography Current Opinion in Cardiology 2002, 17:443–454

58) Soo-Jin Kang, MD, Eun Young Lee, RDCS, Assessment of Papillary Muscle Function in Patients with Inferior Wall Myocardial Infarction Using Doppler Tissue Imaging Journal of the American Society of Echocardiography August 2005

59 Matsuzaki M, Yonezawa F, Toma Y, et al. Experimental mitral regurgitation in ischemia-induced papillary muscle dysfunction. J Cardiol 1988;18 Suppl:121– 6.

60. Miller GE, Jr., Kerth WJ, Gerbode F. Experimental papillary muscle infarction. J Thorac Cardiovasc Surg 1968;56:611– 6.

61 Mittal AK, Langston M, Jr., Cohn KE, Selzer A, Kerth WJ.Combined papillary muscle and left ventricular wall dysfunction as a cause of mitral regurgitation. An experimental study. Circulation 1971;44:174–80.

62 Kaul S, Spotnitz WD, Glasheen WP, Touchstone DA. Mechanism of ischemic mitral regurgitation. An experimental evaluation. Circulation 1991;84:2167– 80.

63 Izumi S, Miyatake K, Beppu S, et al. Mechanism of mitral regurgitation in patients with myocardial infarction: a study using real-time two-dimensional Doppler flow maging and echocardiography. Circulation 1987;76:777– 85.

64 Ogawa S, Hubbard FE, Mardelli TJ, Dreifus LS. Cross-sectional echocardiographic pectrum of papillary muscle dysfunction. Am Heart J 1979;97:312–21.

65 Godley RW, Wann LS, Rogers EW, Feigenbaum H, Weyman AE. Incomplete mitral leaflet closure in patients with papillary muscle dysfunction. Circulation 1981;63:565–71.

68 Soo-Jin Kang, MD, Eun Young Lee, RDCS, Jae-Kwan Song, MD, Kyung-Hyun Do, MD,

Assessment of Papillary Muscle Function in Patients with Inferior Wall Myocardial Infarction Using Doppler Tissue Imaging J Am Soc Echocardiogr 2005;18:815-820.)

69 Banthit Khankirawatana, MD, Suwanee Khankirawatana, RN, Heidi Mahrous, Assessment of Papillary Muscle Function Using Myocardial Velocity Gradient Derived from Tissue Doppler Echocardiography **(**Am J Cardiol 2004;94:45–49)

70 Tenenbaum A, Leor J, Motro M, et al. Improved posterobasal segment function after thrombolysis is associated with decreased incidence of significant mitral regurgitation in a first inferior myocardial infarction. J Am Coll Cardiol 1995;25:1558–63.

71 Rankin JS, Hickey MS, Smith LR, et al. Ischemic mitral regurgitation. Circulation 1989;79 Suppl I:I116 –21.

72 Liel-Cohen N, Guerrero JL, Otsuji Y, et al. Design of a new surgical approach for ventricular remodeling to relieve ischemic mitral regurgitation:insights from 3-dimensional echocardiography. Circulation 2000;101:2756–63.

73 Hvass U, Tapia M, Baron F, Pouzet B, Shafy A. Papillary muscle sling: a new functional approach to mitral repair in patients with ischemic left ventricular dysfunction and functional mitral regurgitation. Ann Thorac Surg 2003;75:809 –11.

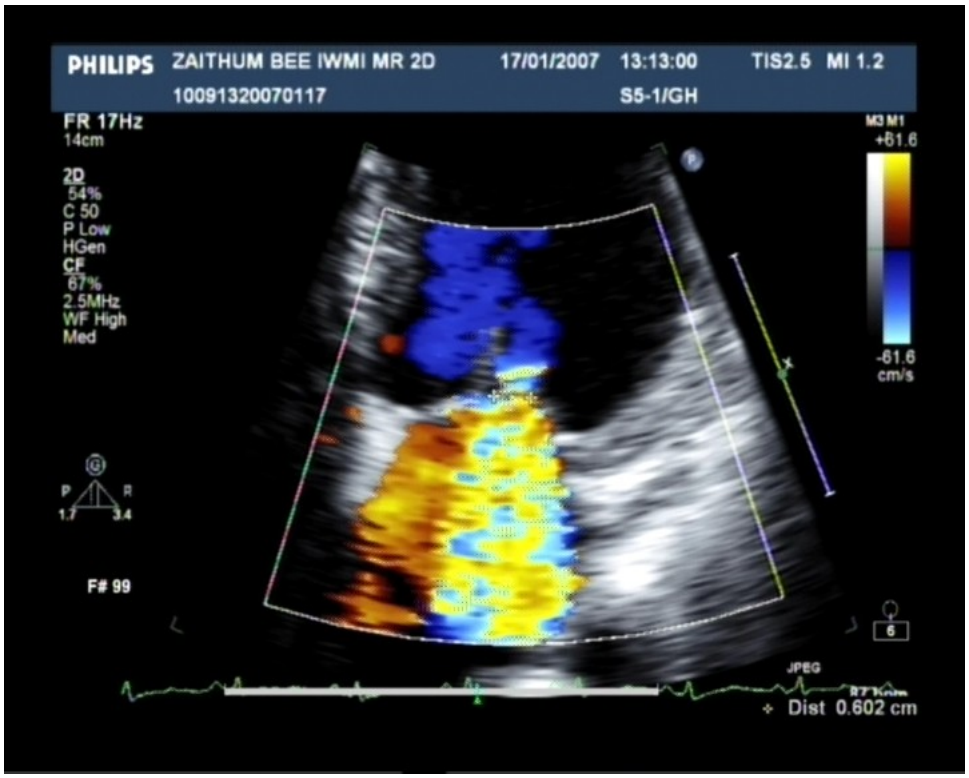
74 Messas E, Guerrero JL, Handschumacher MD, et al. Chordal cutting: a new therapeutic approach for ischemic mitral regurgitation. Circulation 2001;104:1958–63.

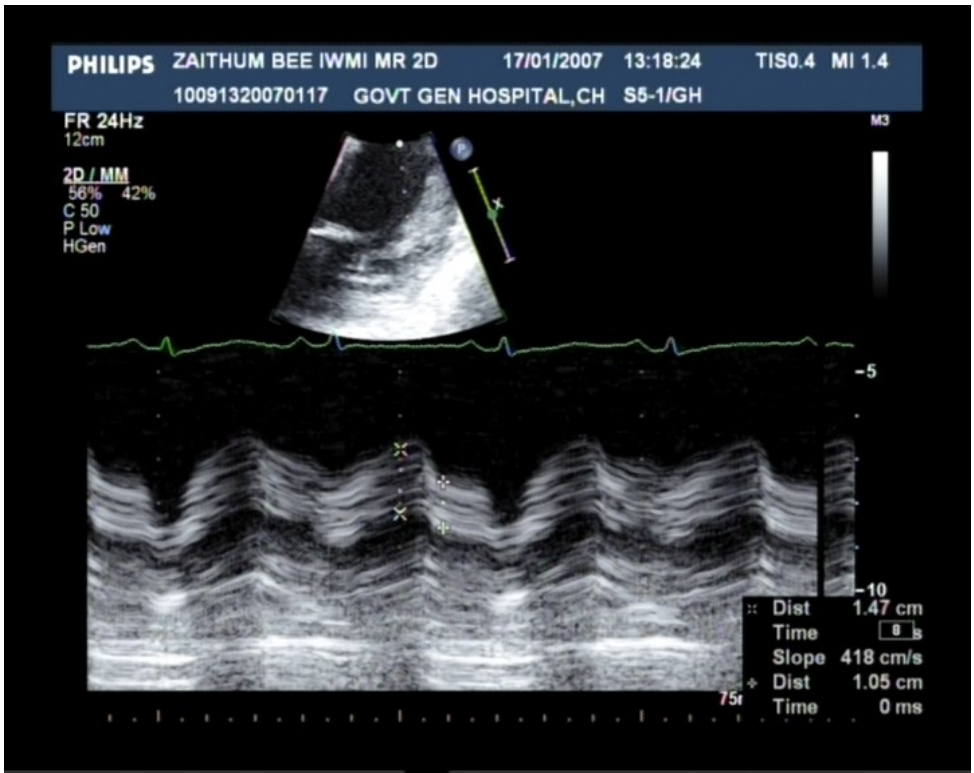
75 Holmes JW, Takayama Y, LeGrice I, Covell JW. Depressed regional deformation near anterior papillary muscle. Am J Physiol 1995;269: H262–70.

GLOSSARY OF ABBREVIATIONS AND ACRONYMS

MR	*Mitral regurgitation*
IMR	*Ischemic Mitral regurgitation*
PM	*Papillary muscle*
PPM	*Posteromedial Papillary muscle*
APM	*Anterolateral Papillary muscle*
AML	*Anterior mitral leaflet*
PML	*Posterior mitral leaflet*
MI	*Myocardial Infarction*
AWMI	*Anterior wall myocardial infarction*
IWMI	*Inferior wall myocardial infarction*
2-D	*Two Dimensional*
ECHO	*Echocardiography*
Am	*Late diastolic velocity*
Em	*Early diastolic velocity*
Sm	*Peak Systolic velocity*
MAA	*Mitral annular area*
LV	*Left Ventricle*
M Mode	*Motion Mode*
TDI	*Tissue Doppler imaging*

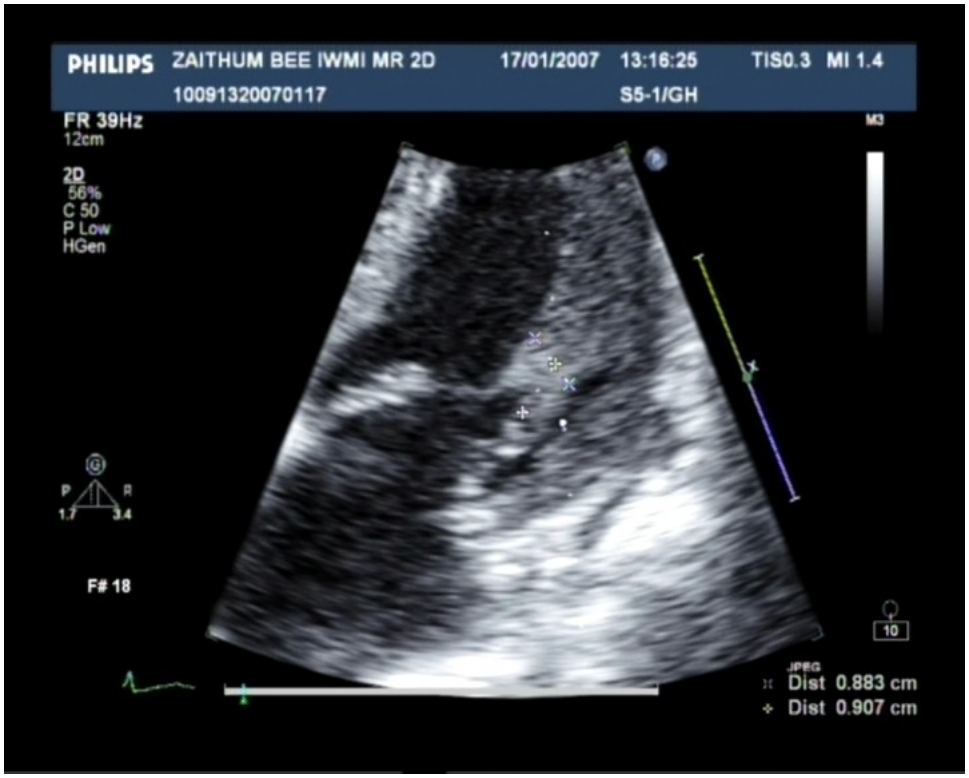
HOCM	*Hypertrophic obstructive cardiomyopathy*
TGA	*D Transpostion of graet artery*
ALCOPA	*Anomolus origion of left coronary from pulmonary artery*
RHD	*Rheumatic heart diseases*
IE	*Infective endocarditis*

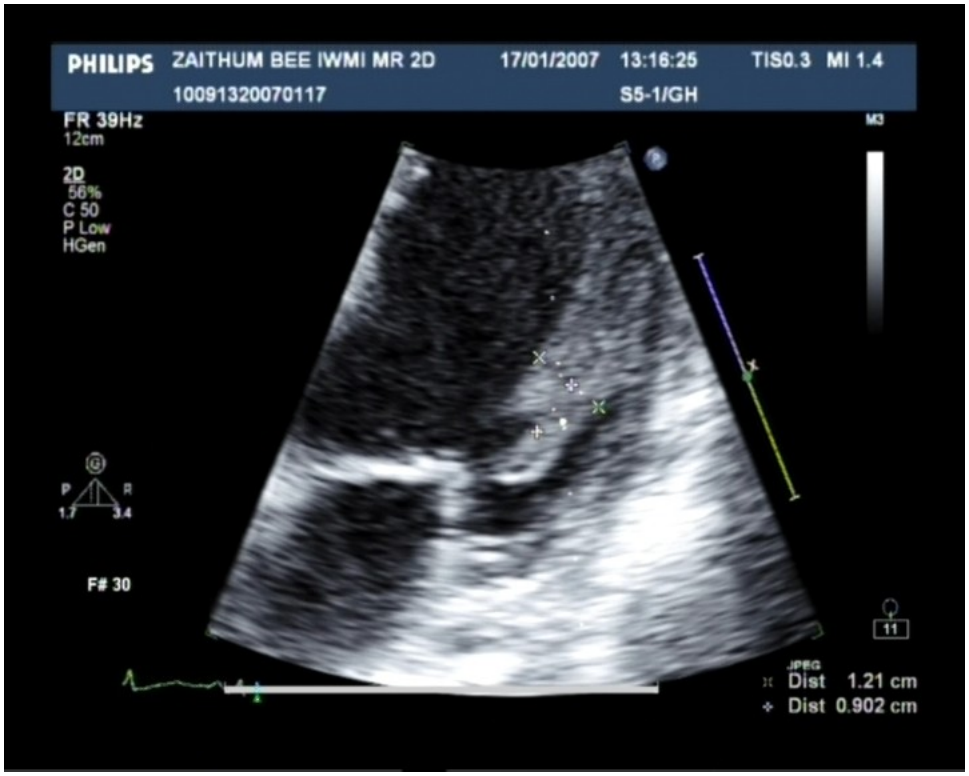




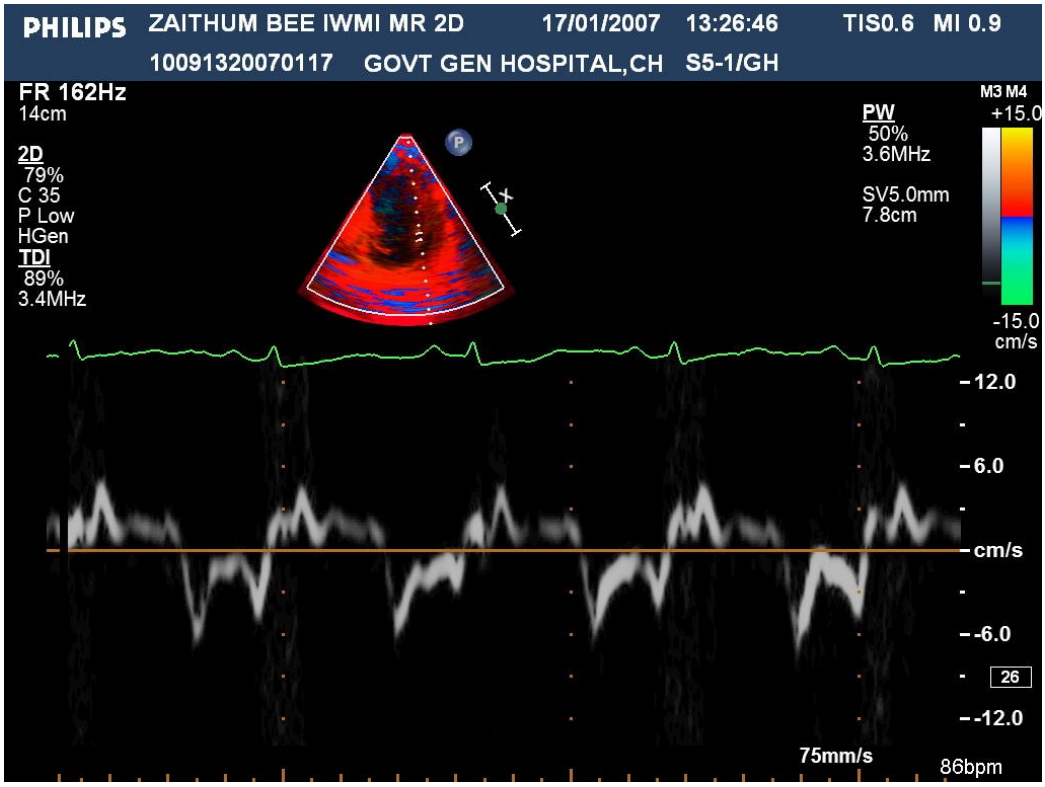
This picture shows severe MR in patient with INFERIOR WALL MI

This picture shows normal systolic thickening of posterior medial papillary muscle in M MODE echo in IWMI with severe MR

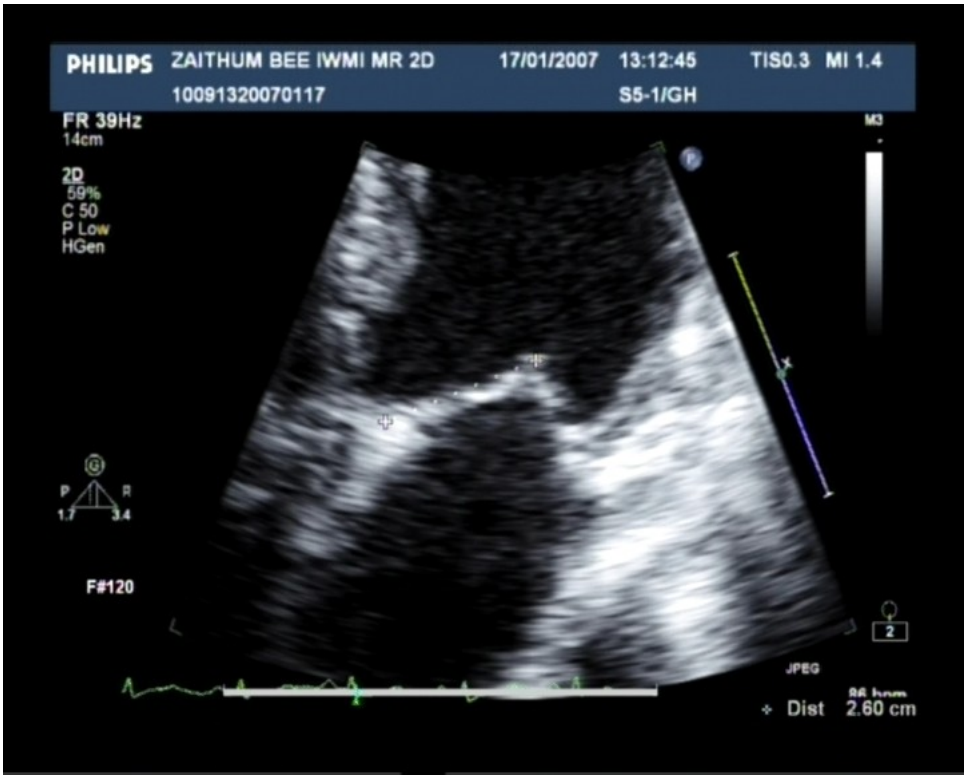




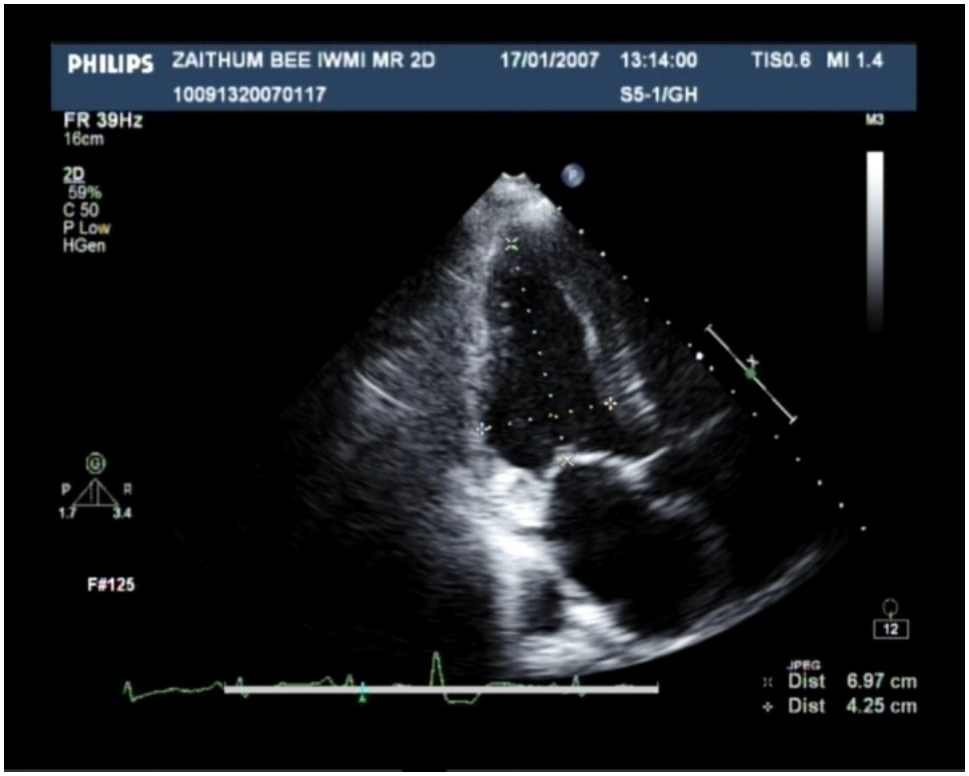
This picture shows normal systolic thickening of posterior medial papillary muscle in 2 D echo in IWMI with severe MR



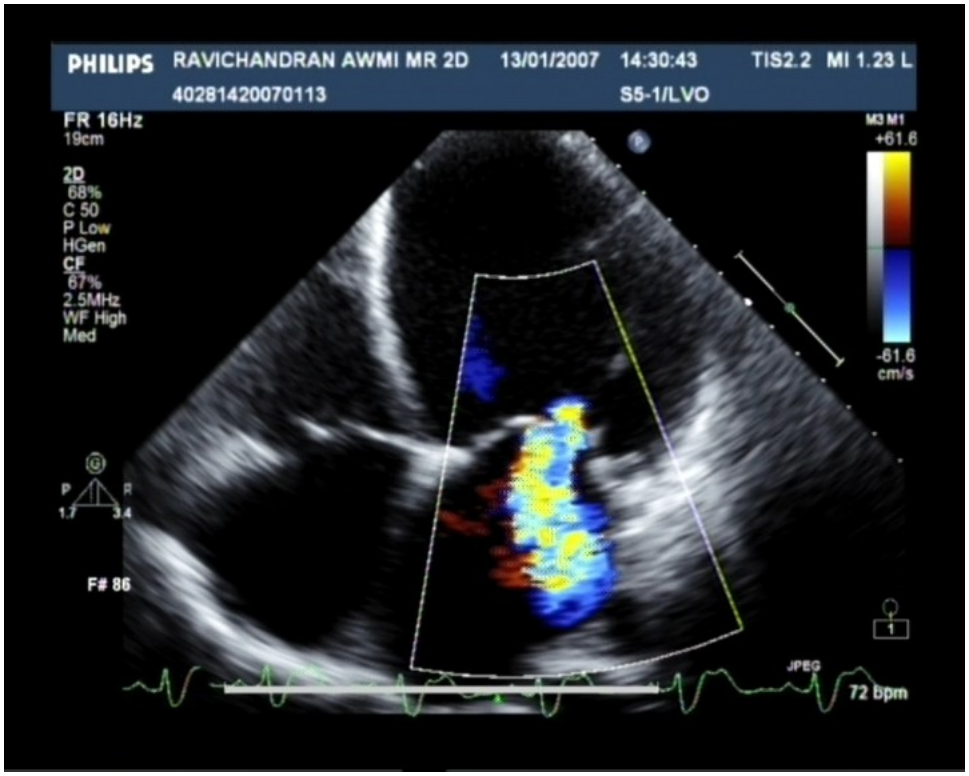
TDI study of Posteromedial papillary muscle shows near normal systolic velocity in IWMI with Severe MR.



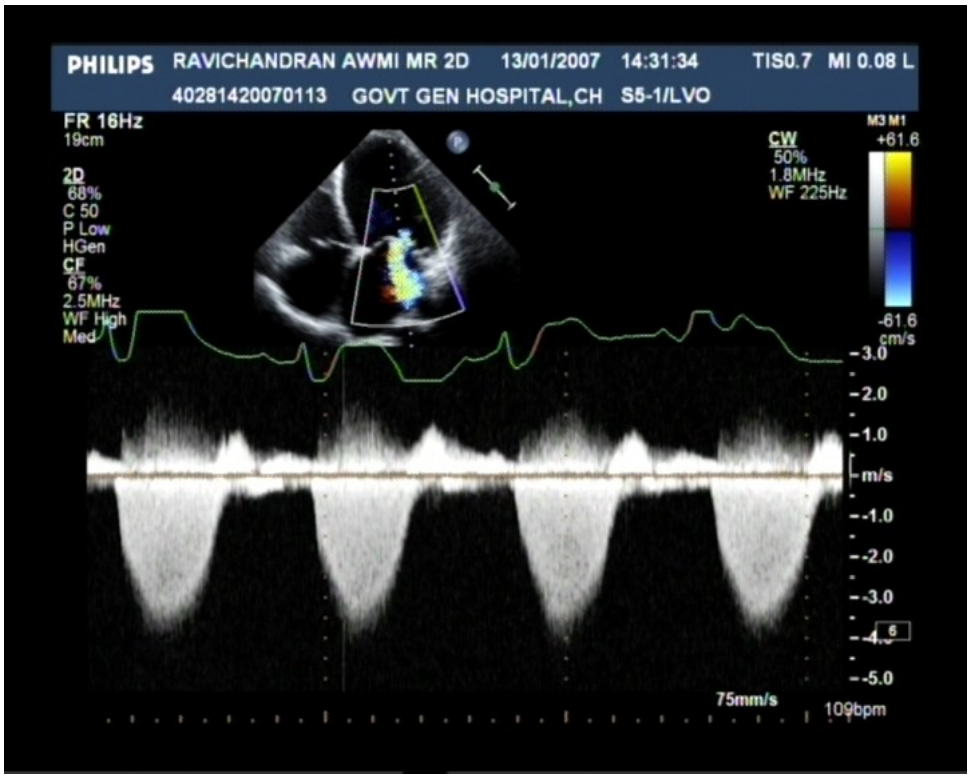
This picture shows increased posterior mitral leaflet tethering distance in IWMI with severe MR.



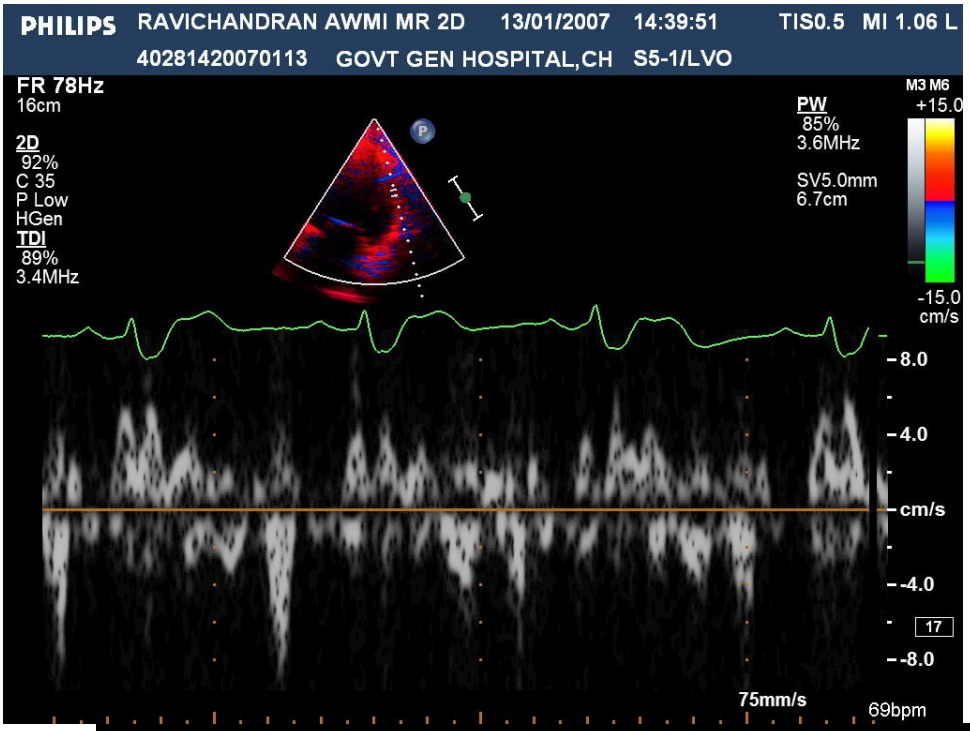
This picture shows increased left ventricular sphericity in IWMI with severe MR



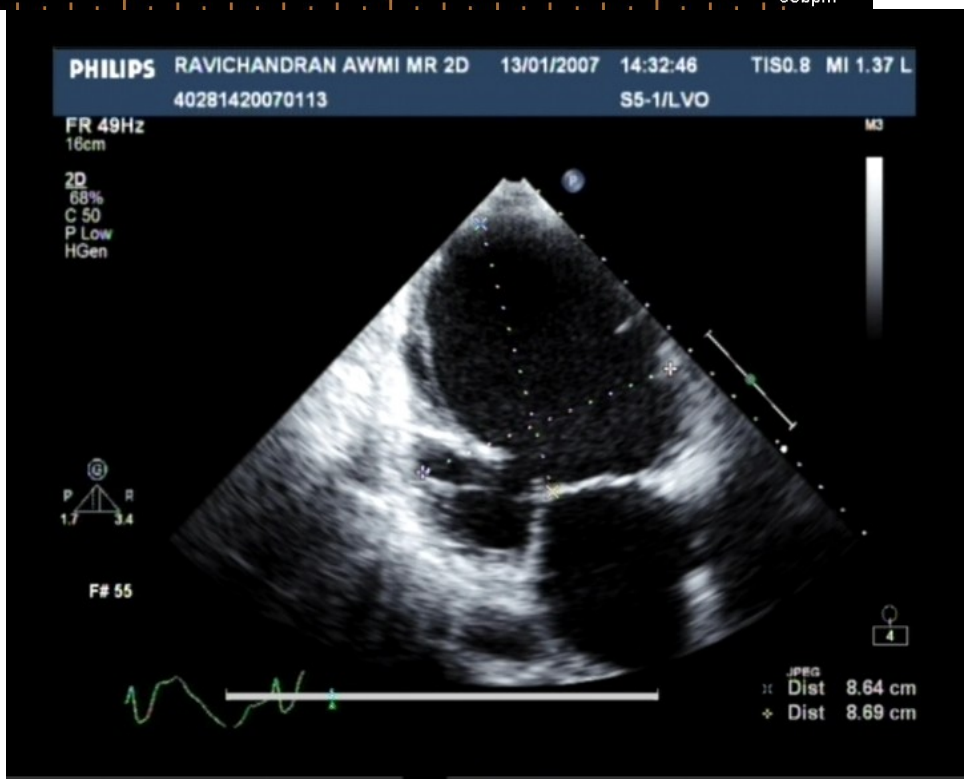
This picture shows severe MR in CF Echo in patient with ANTERIOR WALL MI (AWMI)



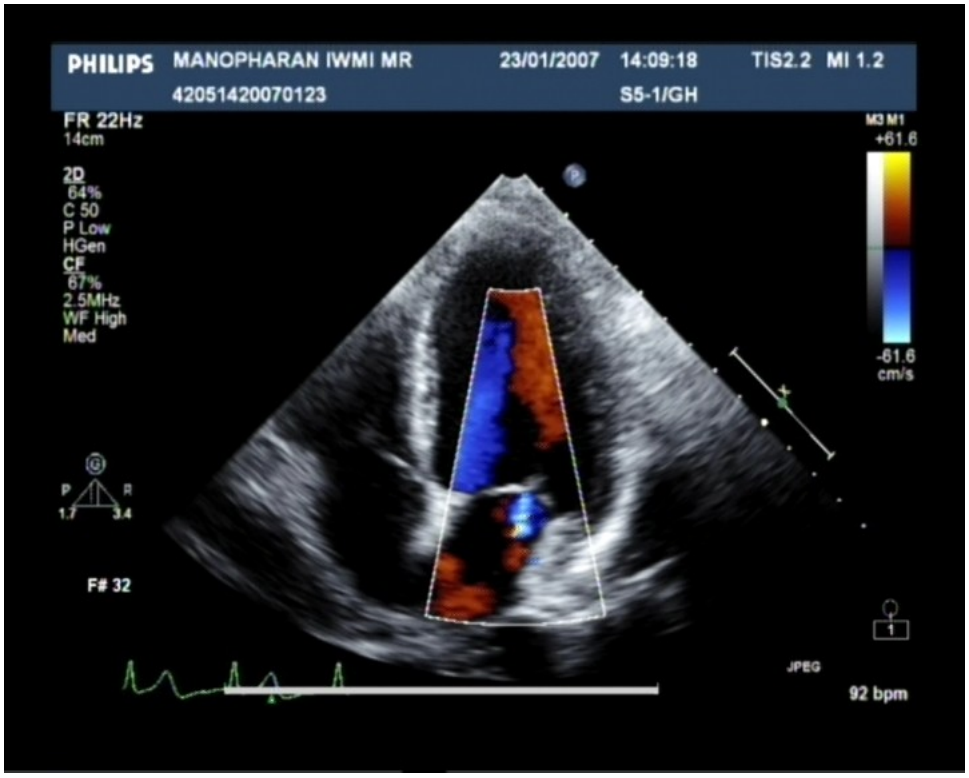
This picture shows severe MR in CWD Echo in patient with ANTERIOR WALL MI (AWMI)



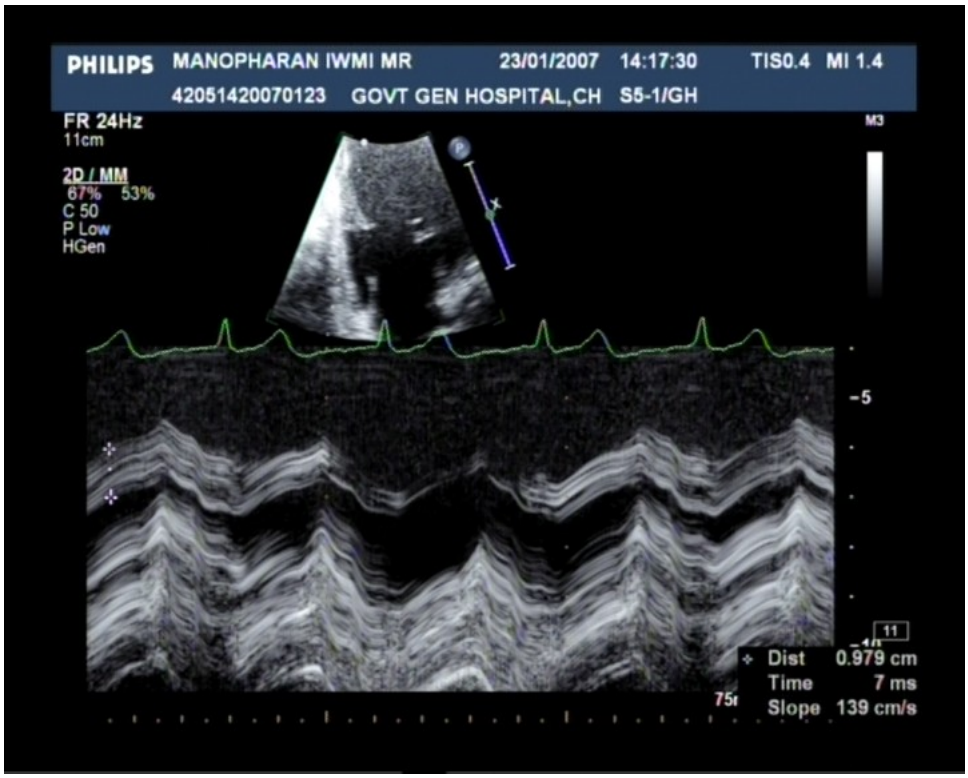
This picture depicts TDI study of anterolateral papillary muscle in AWMI with severe MR



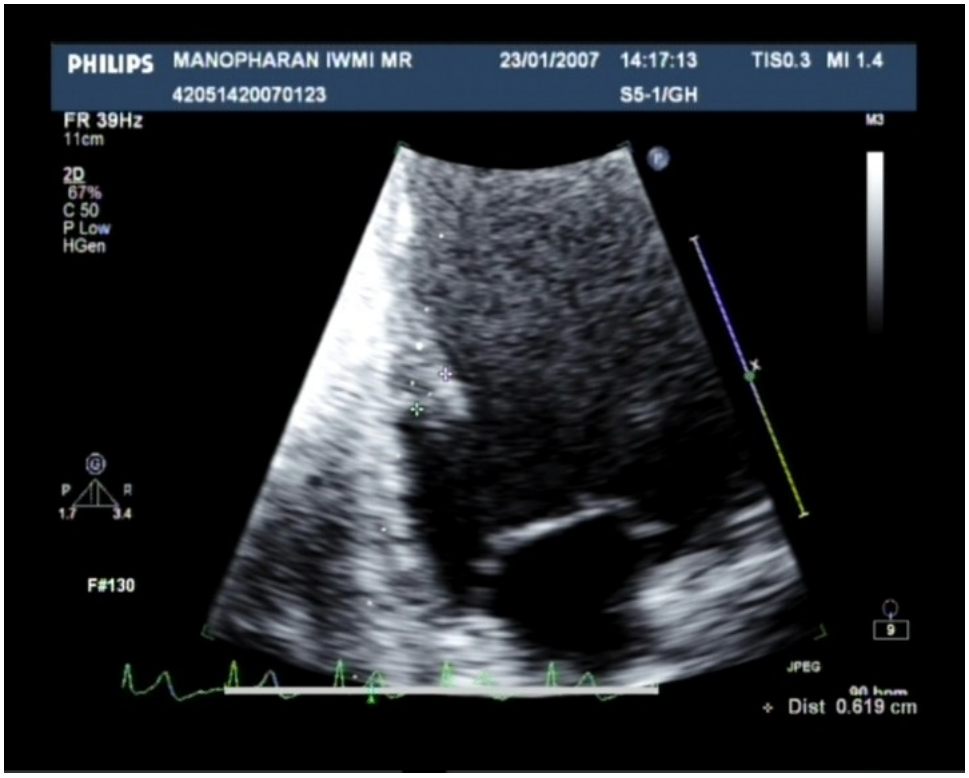
This picture shows increased left ventricular sphericity in AWMI with severe MR



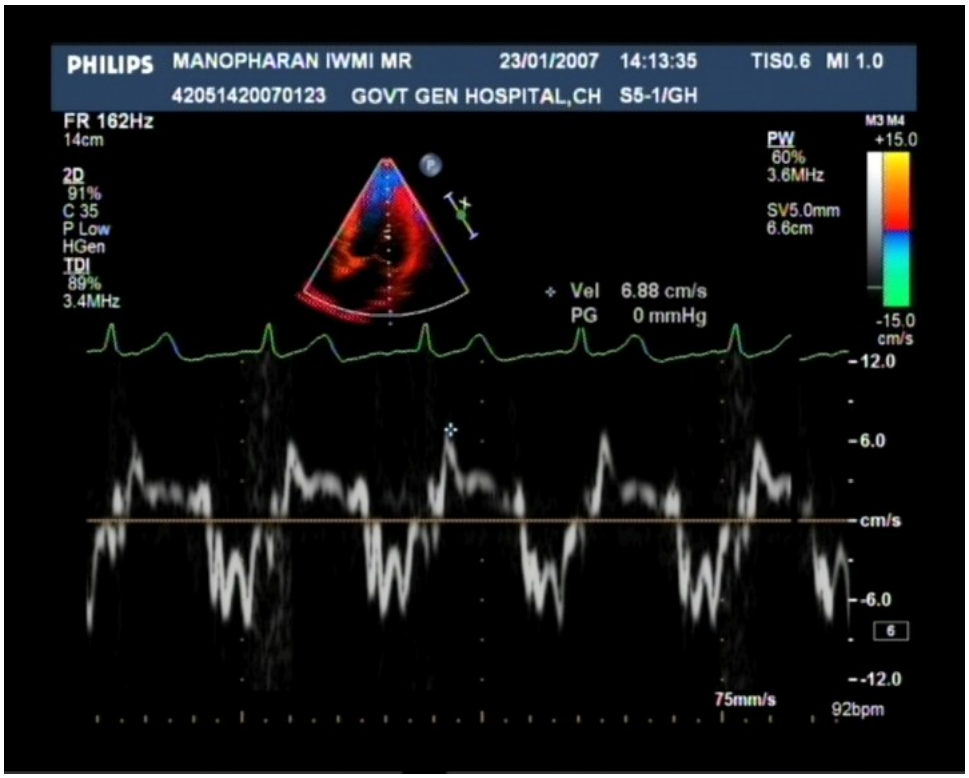
This picture shows mild MR in patient with INFERIOR WALL MI



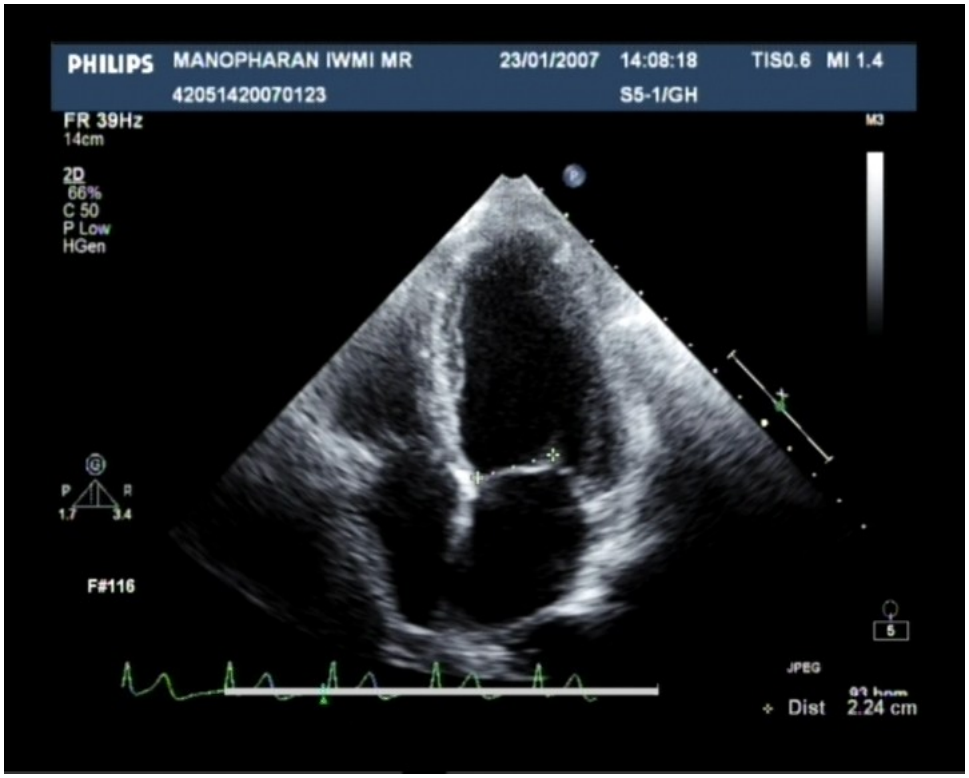
This picture shows reduced systolic thickening of posteromedial papillary muscle in M MODE echo in IWMI with mild MR



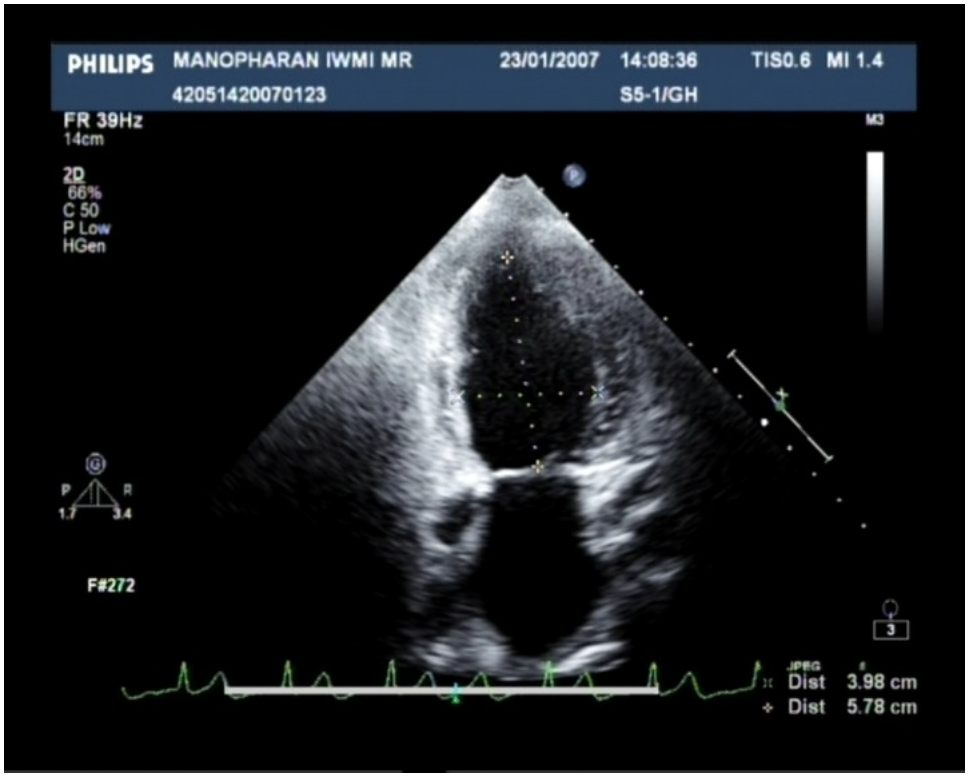
This picture shows reduced systolic thickening of Posteromedial papillary muscle in 2D echo in IWMI with mild MR



TDI study of Posteromedial papillary muscle shows reduced systolic velocity in IWMI with mild MR.

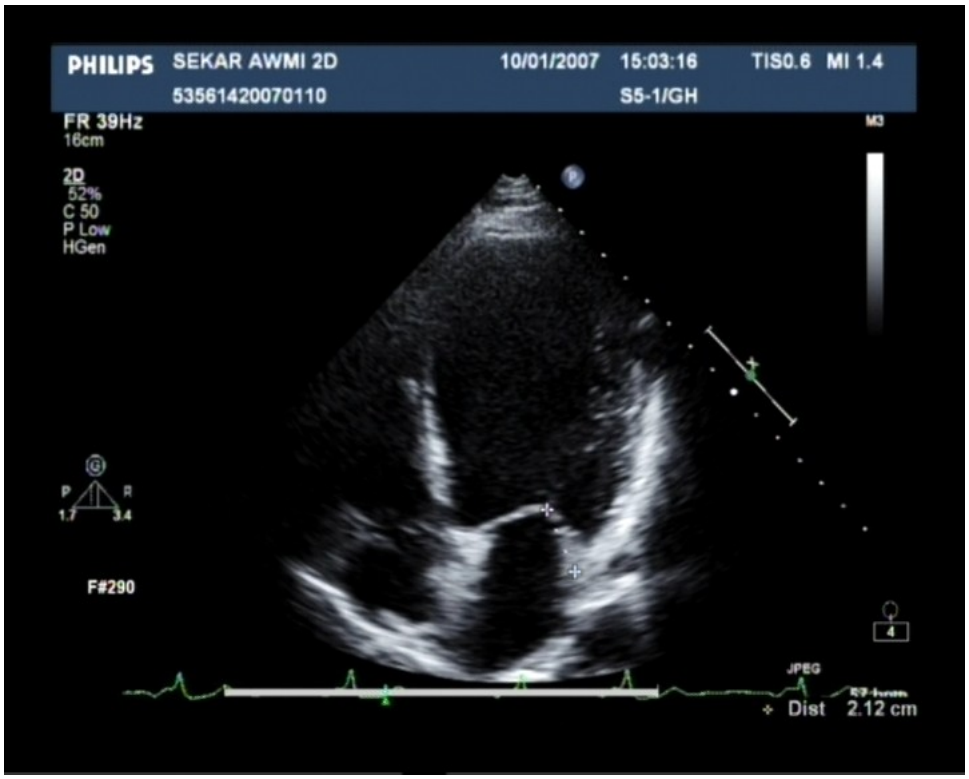


This picture shows posterior mitral leaflet tethering distance in IWMI with mild MR

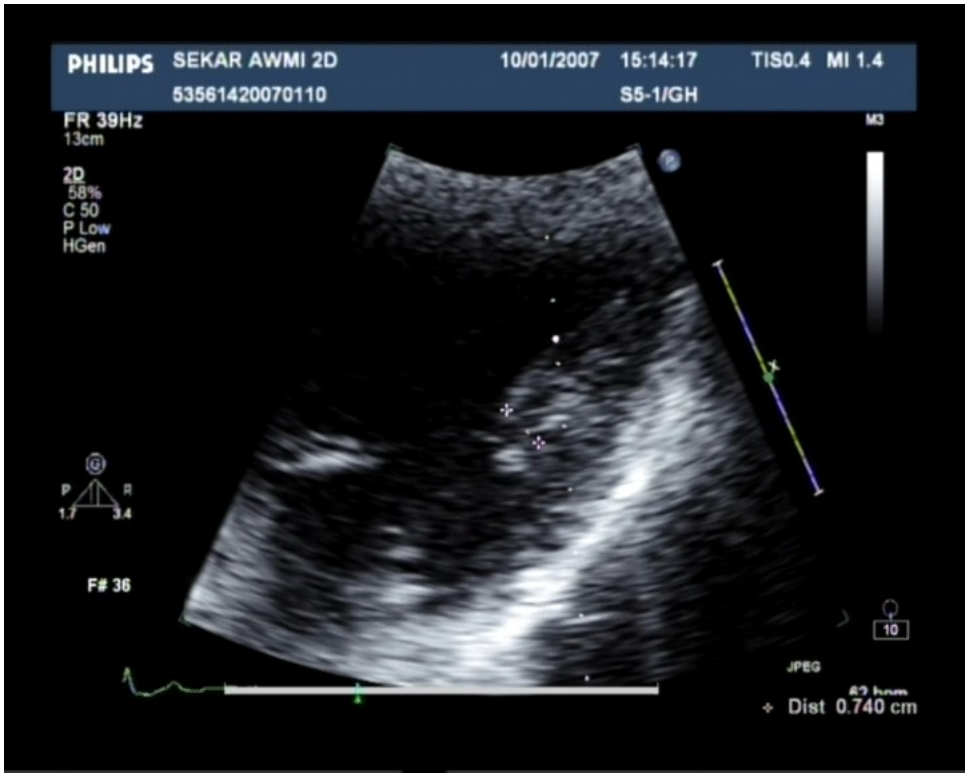


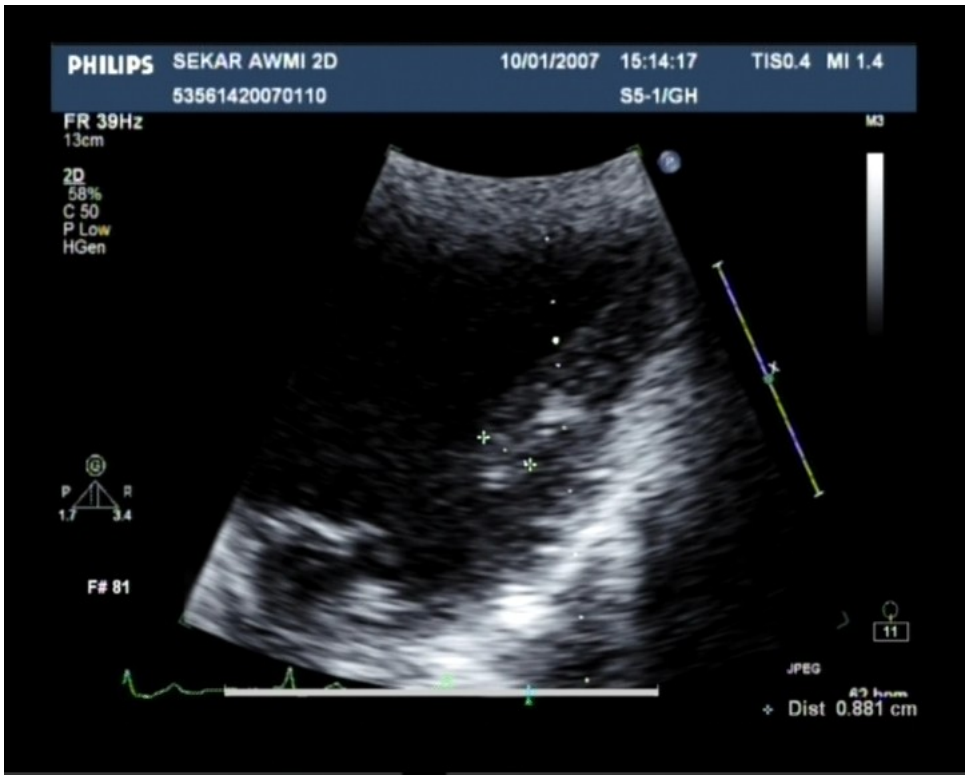
This picture shows normal left ventricular sphericity in IWMI with mild MR

This picture shows mild MR in CF Echo in patient with ANTERIOR WALL MI (AWMI)

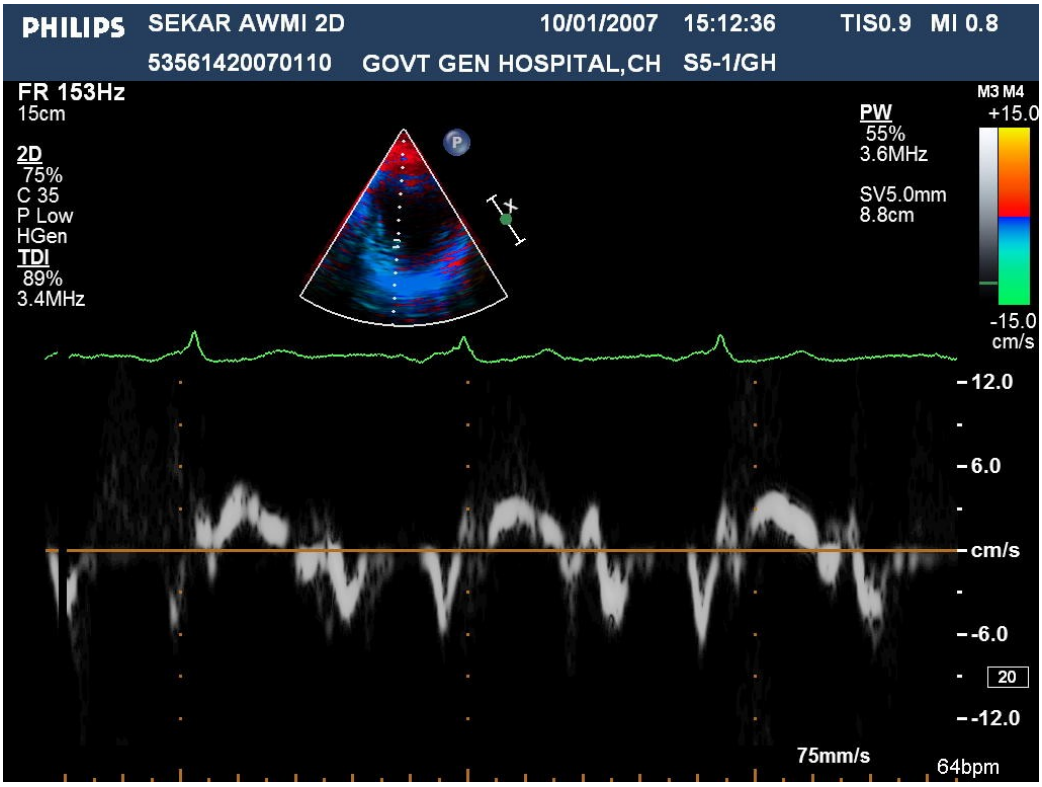


This picture shows anterior mitral leaflet tethering distance in AWMI with mild MR





This picture shows reduced systolic thickening of Anterolateral papillary muscle in 2 D echo in AWMI with mild MR



This picture shows TDI study of Anterolateral papillary muscle in AWMI with mild MR.

PROFORMA

Name :

Age :

Sex :

Address :

CD No. :

History

1. Chest Pain
2. Dyspnoea
3. Palpitation
4. Fatigue

Risk Factors

Hypertension

Diabetes Mellitus

Dyslipidaemia

Sedentary Lifestyle

Smoking

Family History

Obesity

Alcohol Intake

Menopause

Past History of Coronary Artery Disease

Treatment History

Physical Examination

1. General Examination

2. Vital Signs

B.P

Pulse

Respiration

JVP Height cm Waveform

3. Systemic Examination

CVS

Inspection / Palpation

Apex Parasternal Heave

Palpable Sounds Thrills

Auscultation S1 S2 Murmurs

Extra Heart Sounds

Other System

RS: PA: CNS :

Investigations

1. Complete Blood Count P.Glucose

2. B. Urea S. Creatinine

3. S. Electrolytes Ck/Ck MB

4. Chest Roentgenogram PA – View:

ECG

Echocadiograohy

Left Ventricle

EDV: ESV: EF:

RWMA:

LV SPHERICITY :

{D/L in A2c during Mid Systole (D-LV Transverse Diameter, L-LV Longitudinal Diameter}

MAA (MITRAL ANNULUS AREA)

{D1xD2xΠ/4(D1, D2 - Mitral Annuals Diameter in A4c, A2c)

PM TETHERING DISTANCE:

(Tip of PML to Anterior Mitral Annulus, Tip of AML to Posterior Mitral Annulus)

MR VOLUME

PM FUNCTION

M Mode Echo	Pm Diameter	ED
		ES
		Systolic Thickening = $\frac{ES - ED}{ED}$
2D Echo	Pm Diameter	ED
		ES
		Systolic Thickening = $\frac{ES - ED}{ED}$

TDI

APM	Peak Systolic Velocity
	Early Diastolic Velocity
	Late Diastolic Velocity
PPM	Peak Systolic Velocity
	Early Diastolic Velocity
	Late Diastolic Velocity
LV Inferior Wall	Peak Systolic Velocity
	Early Diastolic Velocity
	Late Diastolic Velocity
LV Anterior Wall	Peak Systolic Velocity
	Early Diastolic Velocity
	Late Diastolic Velocity

RESULTS;